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The Chemistry of Malononitrile and its derivatives

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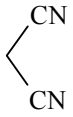
ABSTRACT: Malononitrile is a commonly known and widely used reagent in the synthesis of pharmaceuticals, pesticides, fungicides, solvato-chromic dyes, and organic semiconductors. The unique reactivity of malononitrile promotes more extensive applications of this reagent in organic chemistry even compared to the use of other known CH-acids such as malonic and cyanoacetic esters.

KEYWORDS: malononitrile, aldehydes, ketones, esters, ethers, amines.

1 INTRODUCTION

Malononitrile 1 [1] is used as a key synthons of alkylidenemalononitriles, which contain an activated double bond together with the reactive CN group [2], [3] which is also quite common in organic synthesis. Known reactions in the electrochemistry of alkylidenemalononitriles include cathodic hydrogenation [4] and cyclodim-erization of arylidenemalononitriles, [5] and cathodic addition of alkylidenemalononitriles to acrylonitrile and methyl acrylate.[6]

Malononitrile also considered as very important and useful material, it is used as synthetic substrate for a huge number of compounds e. g. donor-π-acceptor heterocyclic compounds which have recently attracted considerable attention due to their application in ultra fast and ultrasensitive molecular electronic devices and ultrahigh density data storage. [7]



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Malononitrile able to intercalate with Vanadyl phosphate and forms an organic compound has a Lewis base character.[8] malononitrile derivatives such as benzylid-enemalononitrile and its *p*-chloro derivative are used for synthesizing a new class of photo-cross linkable main chain liquid crystalline polymers.[9] A blood group centigenic oligosaccharide monomer containing a benzylidene moiety was chemically synthesized.[9]

Malononitrile derivative such as (E)-2-(3-(4-aminostyryl)-5,5-dimethylcyclo- hex-2-enylidene)malononitrile which is organic non-linear optical (NLO) compound has been intensively studied in recent years because of its potential application in telecommunications and optical information processes 2. [10]

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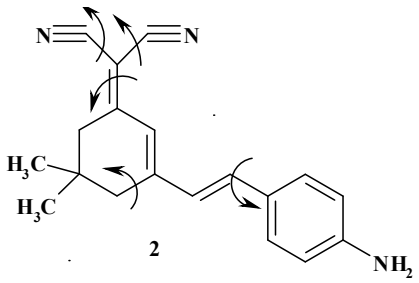
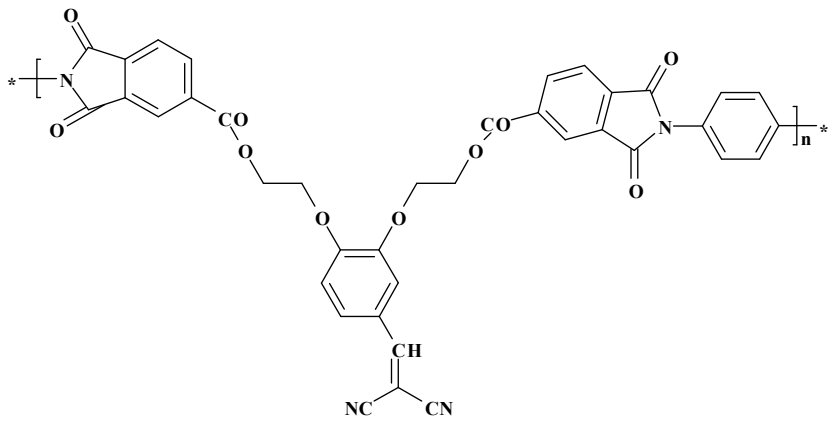


2

In past years, chromophores-functionalized electro-optic (EO) polymeric materials have been intensively investigated for their potential application in high speed photonic devices. This had led to expensive explorations of 'push-pull' type chromophores with high molecular building blocks commonly used for NOL (nonlinear optic) chromophores [11] (electron donor, conjugated bridge and electron acceptor), the development of electron donors and conjugated bridges is already so mature that they can meet most of the synthetic and physical requirements.[11]

Malononitrile derivative (2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofur- an-3-carbonitrile) which is a strong electron acceptor for nonlinear optics [11] was synthesized. It is a molecular building block for NLO material. [11] NOL polymers are considered candidate materials, [6] mainly because they offer many advantages such as mechanical endurance, light weight, and good processability to form optical devices 3, 4. [12]



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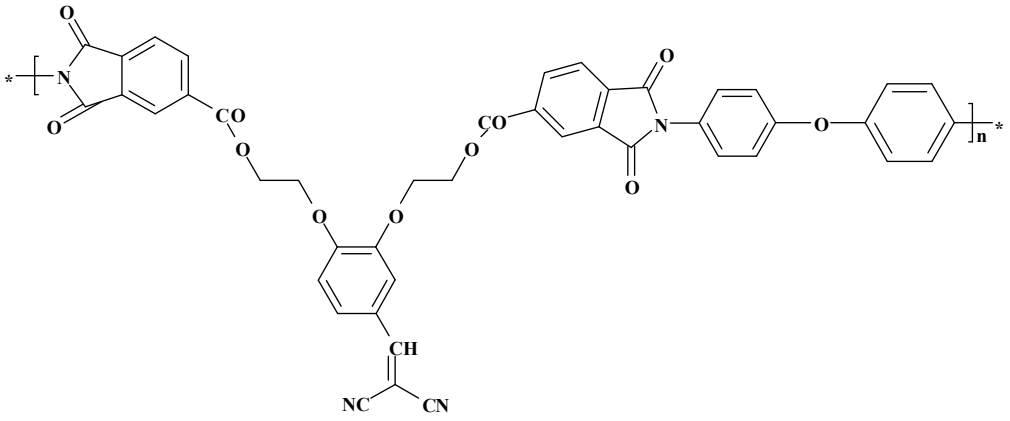
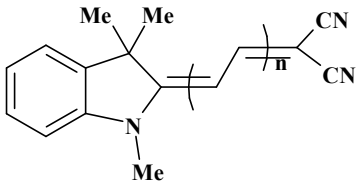


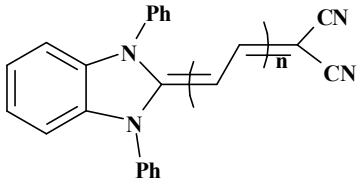
4

The behaviour of the positions and shapes of the fluorescence bands of di-, tetra, and hexamethine merocyanine dyes with 3*H*-indolydine (dyes 5-7) and benzoimidazolyidene (dyes 8-10) as electron-donating substituents and malononit- rile as an electron-accepting substituent is studied by method of moments in solvents of different polarity. [13] Merocyanine dyes

are donor-acceptor compounds exhibiting intermolecular charge transfer from the donor end group through the conjugated polymethine chain. [14] Depending on the charge of these groups [14], [15] and the length of the polymethine chain, as well as the nature of the solvent, the electronic excitation of these compounds can cause either a sharp increase or decrease in their dipole moment. Therefore, the spectral and fluorescent properties of merocyanines are very sensitive to charges in their chemical structure and the polarity of the medium [16], [17]. For this reason, these dyes are widely used in various fields of science and engineering connected with the transformation of light energy. [14-17]

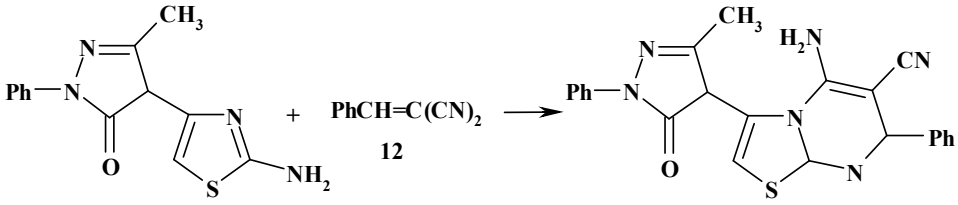


5, n = 1; 6, n= 2; 7, n = 3;



8, n = 1; 9, n = 2; 10, n = 3

Malononitrile derivative such as benzylidenemalononitrile can be used as a precursor for synthesis different heterocycles, which have excellent biocidal properties [18] e. g. 13.



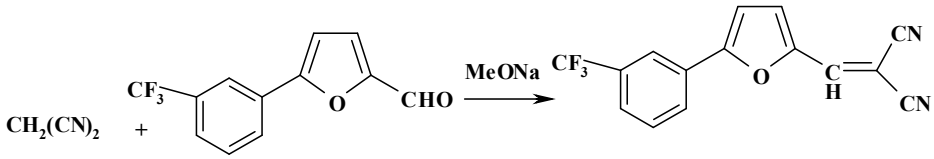
11 **13**

The following study will introduce the chemistry of malononitrile and/or its derivatives.

2 REACTION OF MALONONITRILE AND/OR ITS DERIVATIVES WITH DIFFERENT REAGENTS

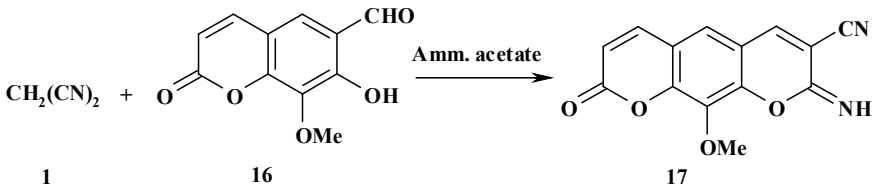
2.1 REACTION WITHALDEHYDES

Reaction of malononitrile 1 with 5-[3-(trifluoromethyl) phenyl]furan-2-carbo-xaldehyde 14 in sodium methoxide resulted in the formation of {5-[3-(trifluoromethyl)phenyl]-2-furyl}methylene malononitrile 15. [19]



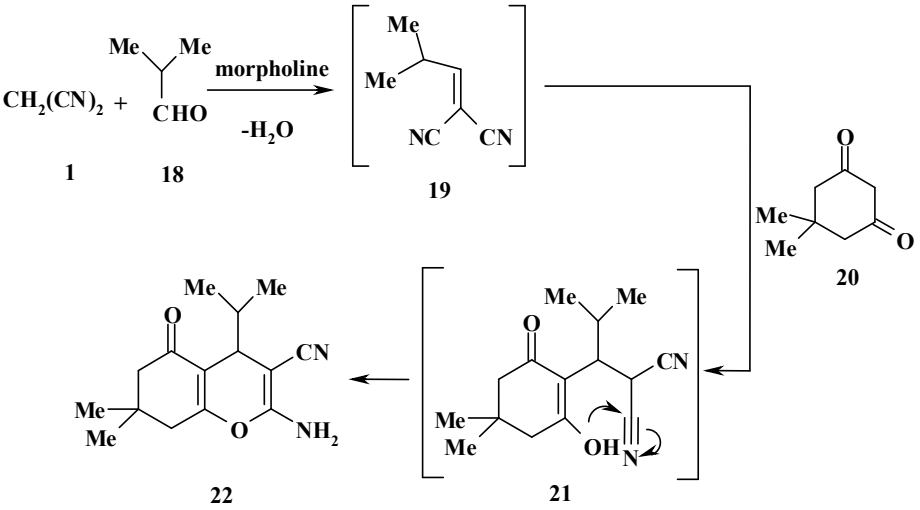
1 **14** **15**

Reaction of malononitrile 1 with 7-hydroxy-8-methoxy-2-oxo-2*H*-1-benzopy- ran-6-carboxaldehyde 16 in the presence of ammonium acetate gives the iminodicoumarin derivative 17. [20]



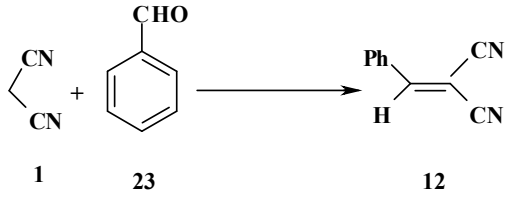
1 16 17

Condensation of malononitrile 1 with isobutyraldehyde 18 in the presence of morpholine gave the adduct 19, which on reaction with dimedone 20 gave 2-amino-4-isopropyl-7,7-dimethyl-5-oxo-5,6,7,8-tetra-hydro-4*H*-chromene-3-carbonitrile 22 *via* the intermediate 21. [21]



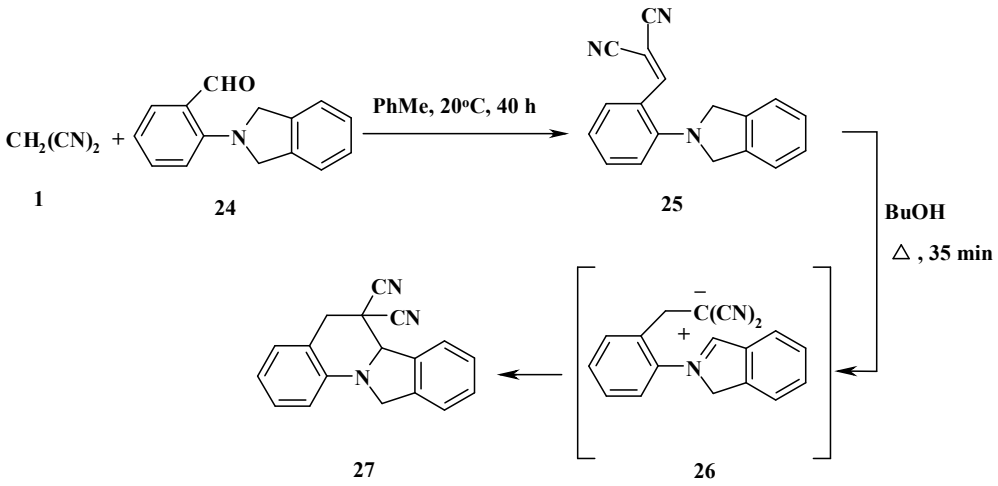
1 18 19 20 21 22

Reaction of malononitrile 1 with benzaldehyde 23 in different reaction conditions gave benzylidenemalononitrile 12. [22-30]



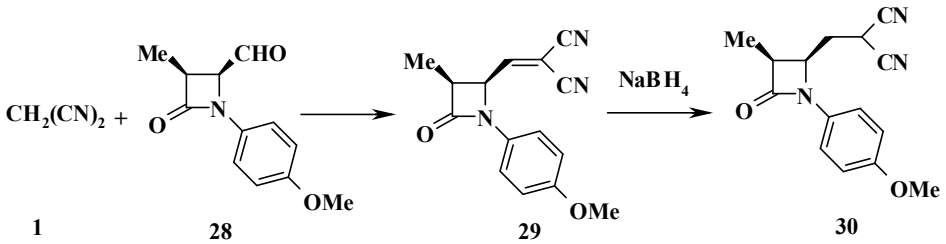
1 23 12

The isoindolo[2,1-*a*]quinoline 27 is formed when the dinitrile 25 boiled in butanol. The initial isoindole 25 is obtained by condensation of the aldehyde 24 with malononitrile 1 in toluene. The cyclization of the benzylidene derivative 25 probably takes place through a [1,5]-shifts of hydrogen and the formation of the dipolar intermediate 26 followed by addition of the carbanion at the iminium fragment. [31]



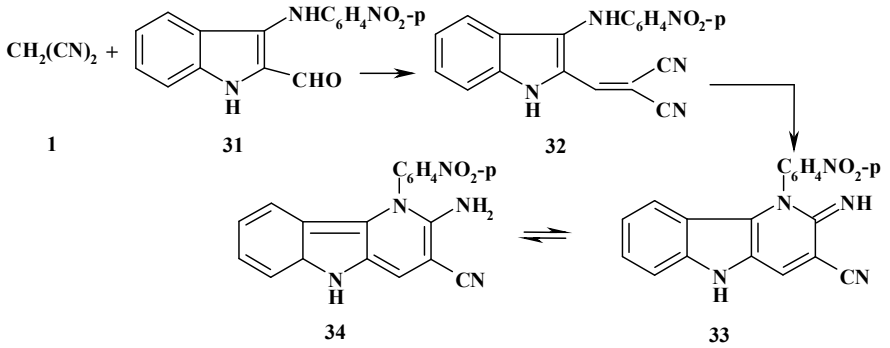
1 24 25 26 27

Condensation of malononitrile 1 with *cis*-4-formyl-1-(4-methoxyphenyl)-3-methyl-2-azetidinone 28 gave the substituted 4-vinyl-1-(4-methoxyphenyl)-3-methyl-2-azetidinone 29. 4-(2,2-dicyanoethy-l)-2-azetidinone 30 was obtained by the catalytic hydrogenation of the double bond in compound 29. [32]



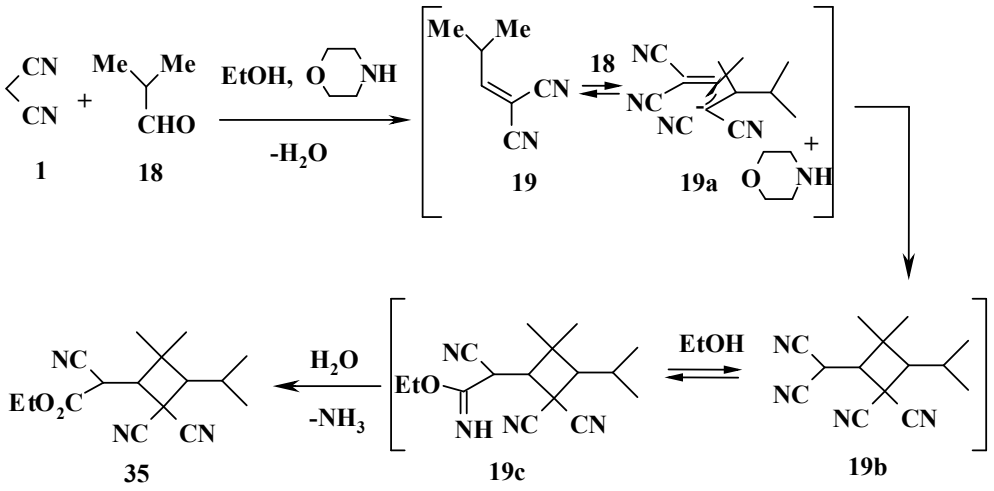
1 28 29 30

2-Formyl-3-*p*-nitrophenylaminoindole 31 reacts with malononitrile 1 to give the dicyanovinyl derivative 32 which is transformed into the corresponding 2-iminodihydropyrido[3,2-*b*] 33 on heating. Compound 33 is in equilibrium with 1-*p*-nitrophenyl-2-amino-3-cyano-1*H*-pyrido[3,2-*b*]indole 34. [33]

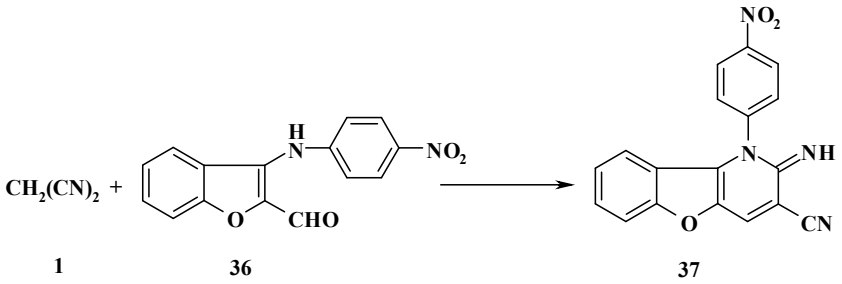


1 31 32 34 33

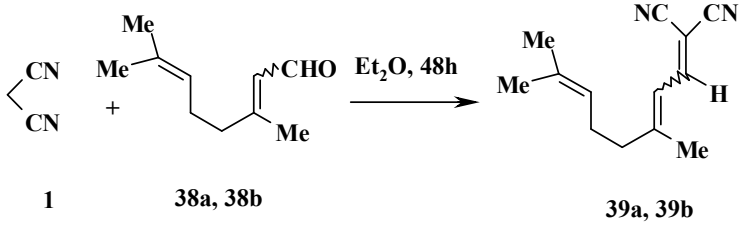
Condensation of malononitrile 1 with isobutyraldehyde 18 in ethanol at 20°C in the presence of morpholine yields substituted cyclobutane 35 *via* intermediates 19-19c. [34]



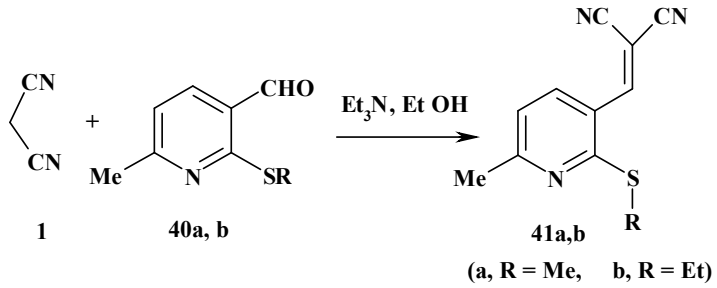
In the reaction of malononitrile 1 with formyl derivative 36 the condensation is accompanied by cyclization with the formation of 3-cyano-2-imino-1-*p*-nitrophenyl-1,2-dihydropyrido[3,2-*b*]benzofuran 37. [35]



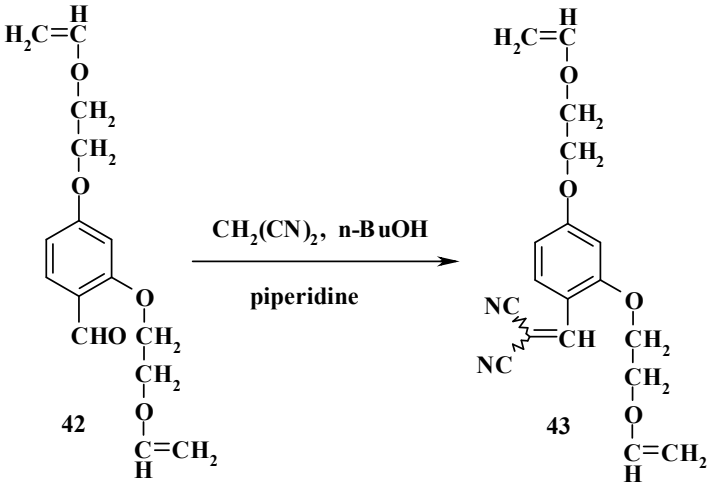
The reaction of malononitrile 1 with monoterpenoid citral (38a/38b, a 1:1 mixture of the *E* and Z isomers) in the presence of basic Csβ-zeolite under mild conditions led to the formation of a mixture of dinitriles 39a, 39b at a ratio of 1:1. [36]



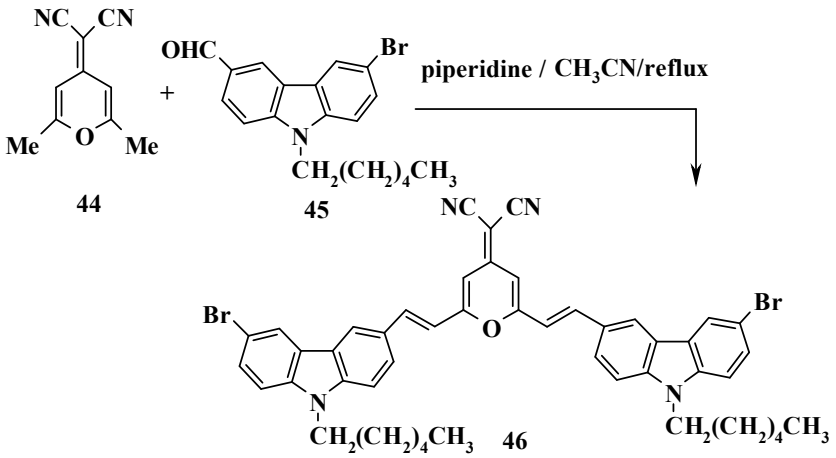
Malononitrile 1 undergoes condensation with 3-formyl-6-methyl-2-methyl-thiopyridine and 2-ethylthio-3-formyl-6-methylpyridine 40a,b to give the corre-spondding ylidene derivatives 41a,b. [37]



Malononitrile 1 reacts with 2,4-di-(2'vinyloxyethoxy)benzaldehyde 42 in *n*-butanol in the presence of piperidine to give 2,4-di-(2'-vinyloxethoxy)benzyliden- emalononitrile 43. [38]

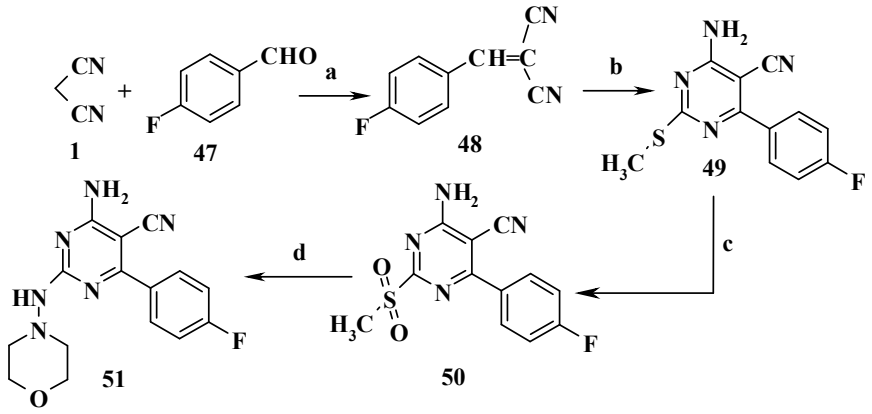


Malononitrile 1 derivative 2-(2-,6-dimethylpyran-4-ylidene)malononitrile 44 reacts with 6-bromo-9-hexyl-9*H*-carbazole-3-carbaldehyde 45 in acetonitrile and piperidine. The reaction solution was stirred at reflux under nitrogen for 24 h to furnish 2-{2,6-bis[2-(6-bromo-9-hexyl-9*H*-carbazol-3-yl)vinyl]pyran-4-ylidene} malononitrile 46, which is used as intermediate in the synthesis of target polymers. [39]



Knoevenagel condensation reaction which was carried out between malononitrile 1 and *p*-fluorobenzaldehyde 47 in the presence of piperidine in ethanol to yield the corresponding benzylidenemalononitriles 48. Compound 48 were cyclised with

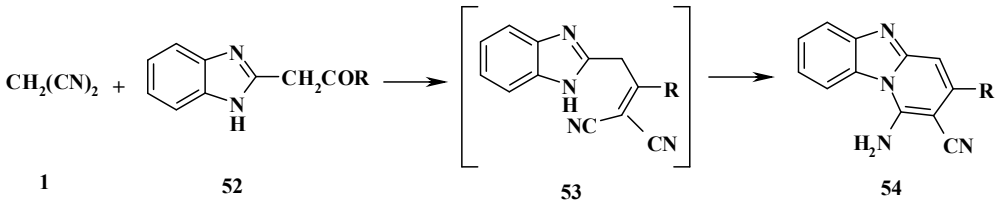
S-methylisothiourea sulfate in the presence of K_2CO_3 in methanol to give 2-thiomethyl-4-amino-5-cyano-6-aryl pyrimidine 49 according to the reported procedure with slight modification. [40], [41] Compound 49 were further oxidized to corresponding sulfone 50 in the presence of *m*-chloroperoxybenzoic acid. The sulfones 50 were subjected to nucleophilic substitution with different amines at refluxing methanol to yield the targeted compound 51. [42]



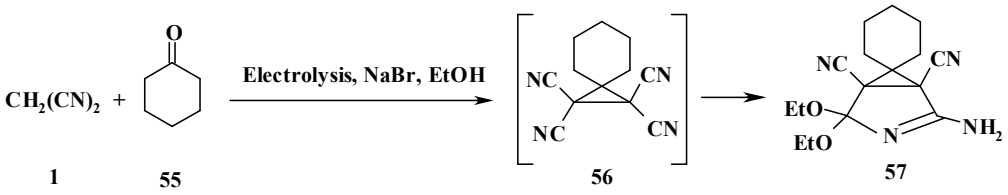
Reagents and conditions: (a) piperidine, ethanol, rt; (b) S-methylisothiourea Sulfate, K_2CO_3, methanol, reflux, 5h; (c) m-CPBA, DCM, O ^{o}C-rt; (d) aminomorpholine.

2.2 Reaction With Ketones

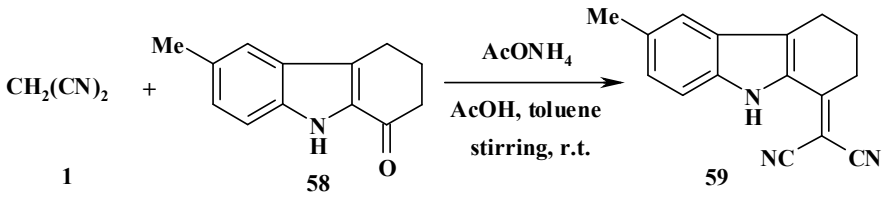
It is found that the reaction of malononitrile 1 with 2-acetonylbenzimidazole 52 does not stop at the stage of formation of the dicyanomethylene derivative 53 but is accompanied by the intramolecular addition of the bezimidazoleimino group to the nitrile giving the 1-amino-2-cyano-3-methylpyrido[1,2-*a*] benzimidazoles 54. [43]



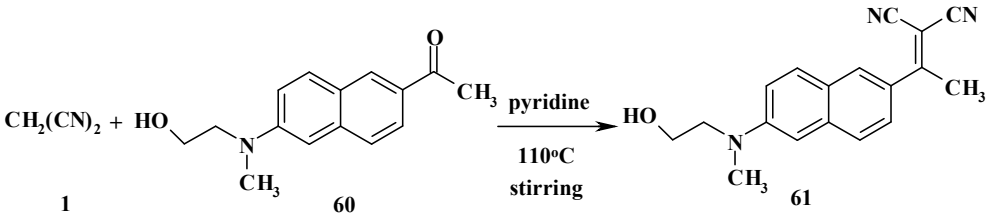
It is found that unexpectedly that in the reaction of malononitrile 1 with cyclohexanone 55 in an electrochemical process cannot stopped after the formation of tetracyanocycloprone 56; co-electrolysis of cyclohexanone and malononitrile under this condition furnishes 2-amin-o-1,5-dicyano-4,4-diethoxy-6,6-pentam- ethylene-3-azabicyclo[3.1.0]hex-2-ene 57. [44]



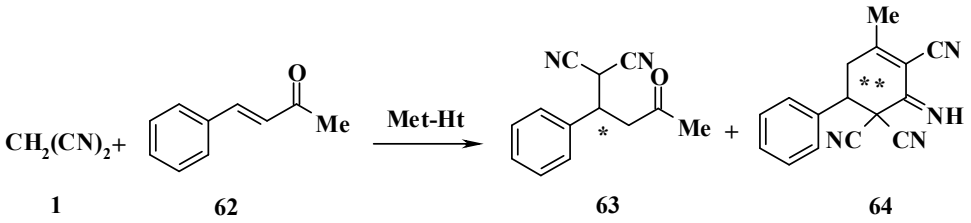
Condensation of malononitrile 1 with 6-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one 58 gave 1-(dicyanomethylene)-6-methyl-2,3,4,9-tetrahydro-1*H*-carbazole 59. [45]



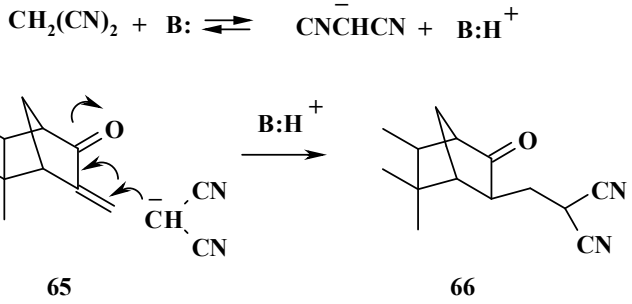
Condensation of malononitrile 1 with 1-{6-[(2-hydroxyethyl) (met-hyl)amino]-2-naphthyl}ethan-1-one 60 in pyridine at 110°C yields 1-{6-[(2-hydroxyethyl) (methyl)amino]-2-naphthyl}ethylidene)malononitrile 61. [46]



Reaction of malononitrile 1 with benzalacetone 62 by using basic chiral catalyst which was prepared by applying cesium methionate to hydrotalcite (natural basic clay), resulted in the formation of optically active products 63 and 64. [47]

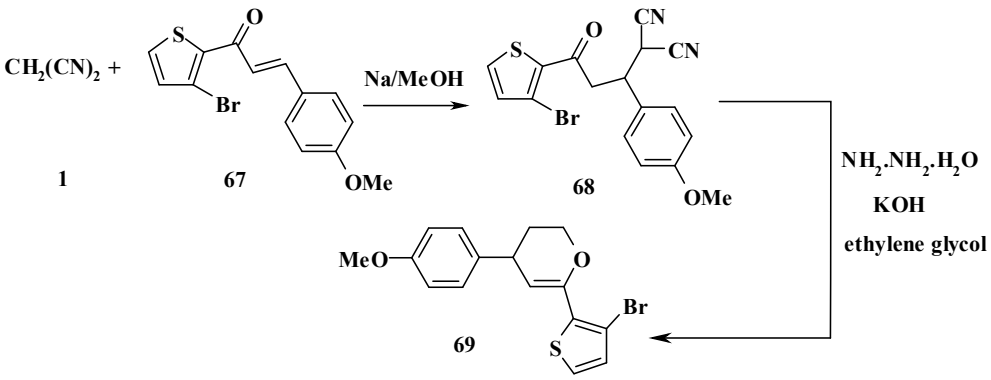


The reaction of malononitrile 1 with 3-methyleneisocamphanone 65 follows Michael reaction when the process is carried out in ethanol, methanol or THF and catalyzed by tetramethylguanidine. As a result arises 3-exo-(2,2-dicyanoethyl) isocamphanone 66. [48]

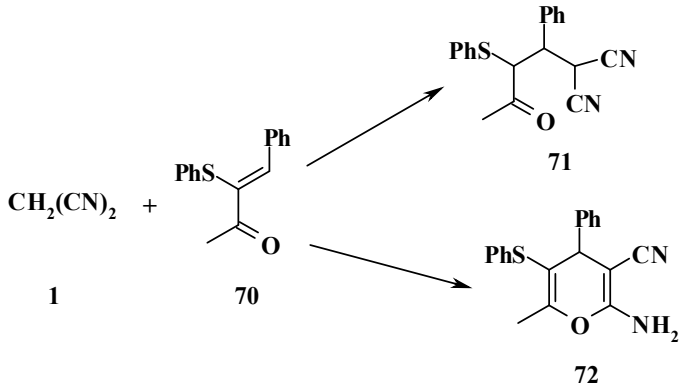


Reaction of malononitrile 1 with 1-(3-bromo-2-thienyl)-3-(4-metho-xyphenyl)-2-propen-1-one 67 in sodium methoxide yielded 5-(3-bromo-2-thienyl)-2-cyano-3-(4-methoxyphenyl)-5-oxovaleronitrile 68.

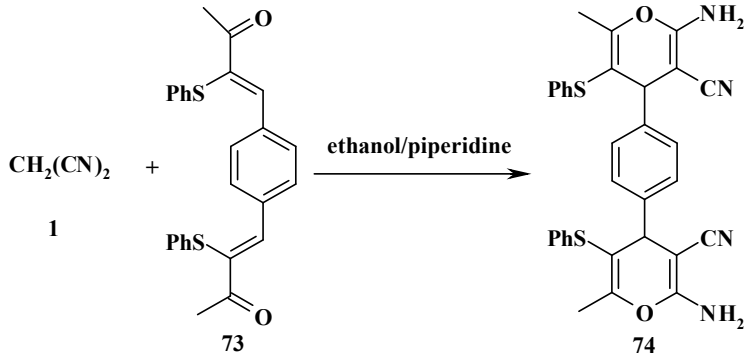
On treating 68 with hydrazine hydrate and KOH in ethylene glycol, (RS)-2-(3-bromo-2-thienyl)-4-(4-methoxyphenyl)-4*H*-5,6-dihydro-pyrane 69 was obtained. [49]



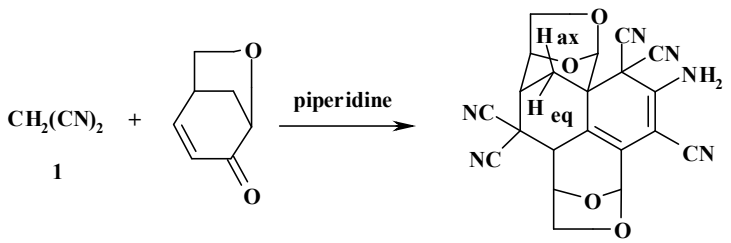
Heating of malononitrile 1 with 3-phenylthio-4-(4-phenyl)-3-buten-2-one 70 in the presence of piperidine in acetonitrile resulted in formation of a complex mixture from which the noncyclic Micheal adduct 2-cyano-5-oxo-3-phenyl-4-(phenylthio)hexanenitrile 71 and the cyclic one 2-amino-6-methyl-4-phenyl-5-(phenylthio)-4*H*-pyran-3-carbonitrile 72 were isolated. [50]



A double Micheal addition of malononitrile 1 to substrate containing two α,β-unsaturated carbonyl groups attached to the benzene ring in positions 1 and 4 was achieved. The reaction of malononitrile 1 with 1,4-bis(3-phenylthio)-3-buten-2-one-4-yl)-benzene 73 in a molar ratio of 2:1 carried out in absolute ethanol and catalyzed by piperidine afforded the desired 1,4-bis-(2-amino-3-cyano-6-methyl-5-(phenylthio)-4*H*-pyran-4-yl)benzene 74. [50]

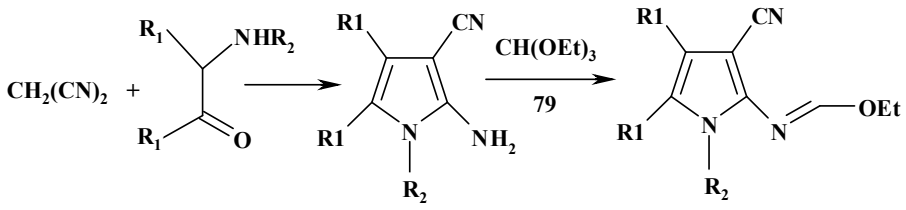


Malononitrile 1 reacts with an equimolar amount of levoglucosenone 75 in the presence of piperidine to form a product to which structure 76. [51]



75 76

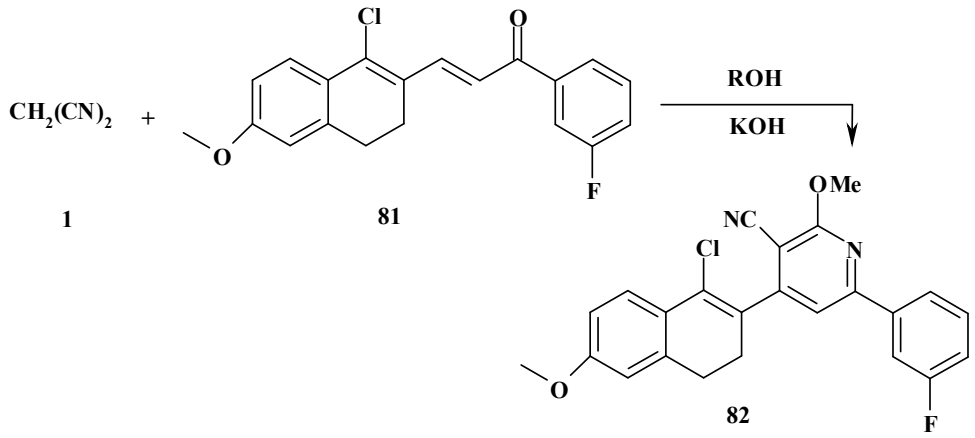
Condensation of malononitrile 1 with amino ketones 77a-c afforded the adducts 78a-c. Refluxing of aminonitriles 78a-c with triethylorthformate 79 over a short period of time afforded imidic esters 80a-c. [52]



1 77a-c 78a-c 80a-c

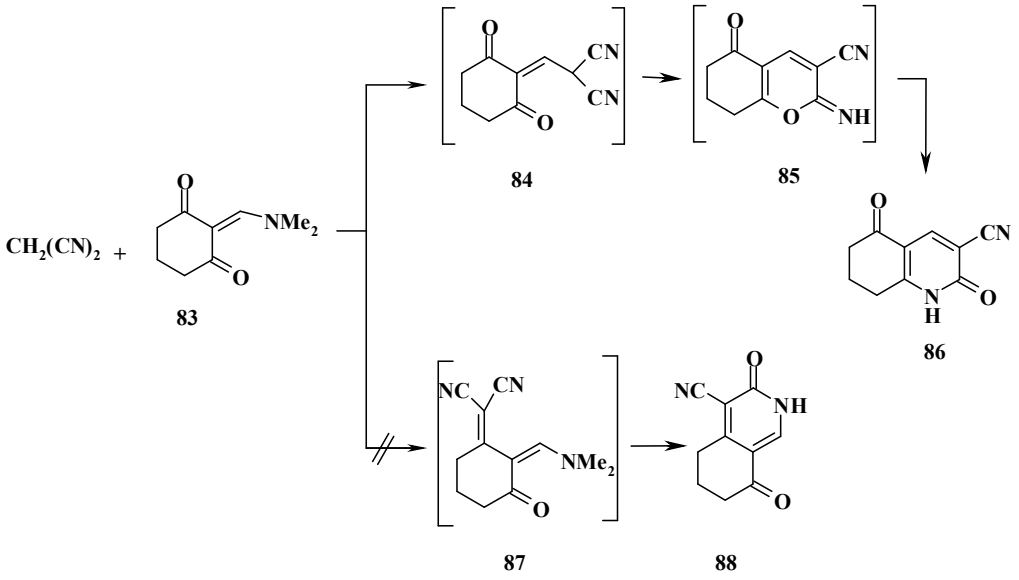
	R1	R2
a	Me	3-pyridyl
b	Ph	Bn
c	Me	2-furfuryl

Condensation of malononitrile 1 with (2*E*)-3-(1-chloro-6-methoxy-3,4-dihydronaphthalen-2-yl)-1-(4-fluorophenyl)prop-2-en-1-one 81 in alcohol containing a catalytic amount of potassium hydroxide with stirring at 30-35^{o}C for 14h yielded the corresponding 4-(1-chloro-6-methoxy-3,4-dihydronaphthalen-2-yl)-6-(4-fluorophenyl)-2-methoxynic-otinonitrile 82. [53]

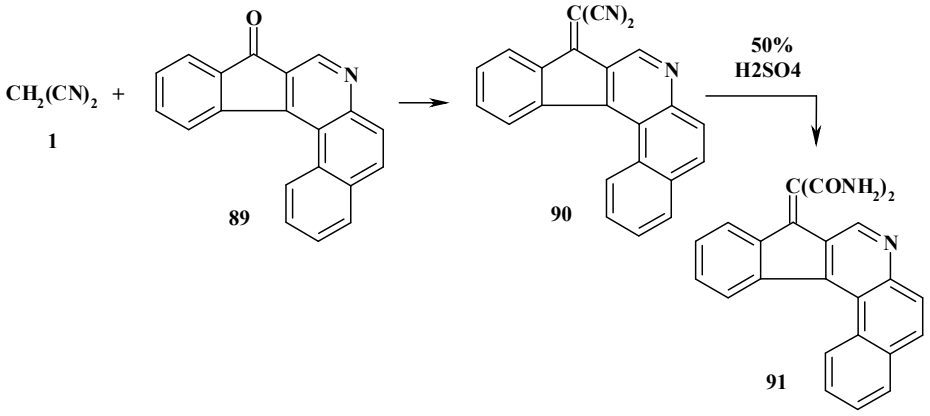


1 81 82

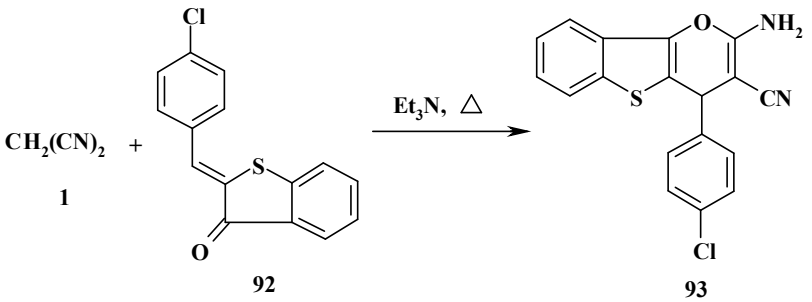
Reaction of malononitrle 1 with 2-dimethylaminomethylenecyclohexane-1,3-dione 83 in refluxing acetic acid and in presence of ammonium acetate yielded product *via* dimethylamine elimination. This can be formulated as 84-88. [54]



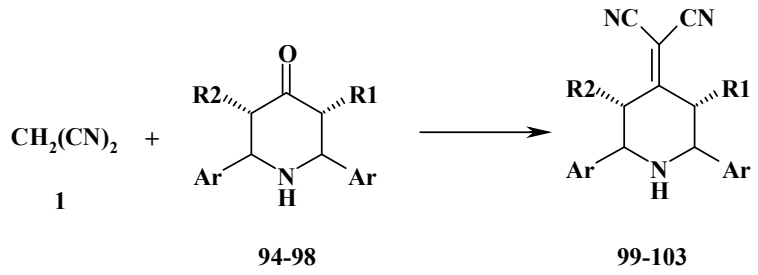
Condensation of malononitrile 1 with 7-azaindeno[2,1-*c*]phenathren-9-one 89 was performed in a mixture of 1:1 DMF-pyridine and by heating under reflux for 20-25 min. The adduct 2-(7-azaindeno[2,1-*c*]phenathren-9-ylidene)-propanedinitrile 90 was obtained. The adduct 90 can be transformed into 2-(7-azaindeno[2,1-*c*]phenathren-9-ylidene)propanediamide 91 by action of diluted sulfuric acid and heating for 25-30 min on a boiling water bath. [55]



On heating malononitrile 1 with 2-(*p*-chlorophenyl)methylidene-1-benzothioph- ene-3(2*H*)-one 92 in EtOH in the presence of Et_3N produces 2-amino-4-(*p*-chloro- phenyl)-4*H*-[1]benzothieno[3,2-*b*] pyran-3-carbonitrile 93. [56]



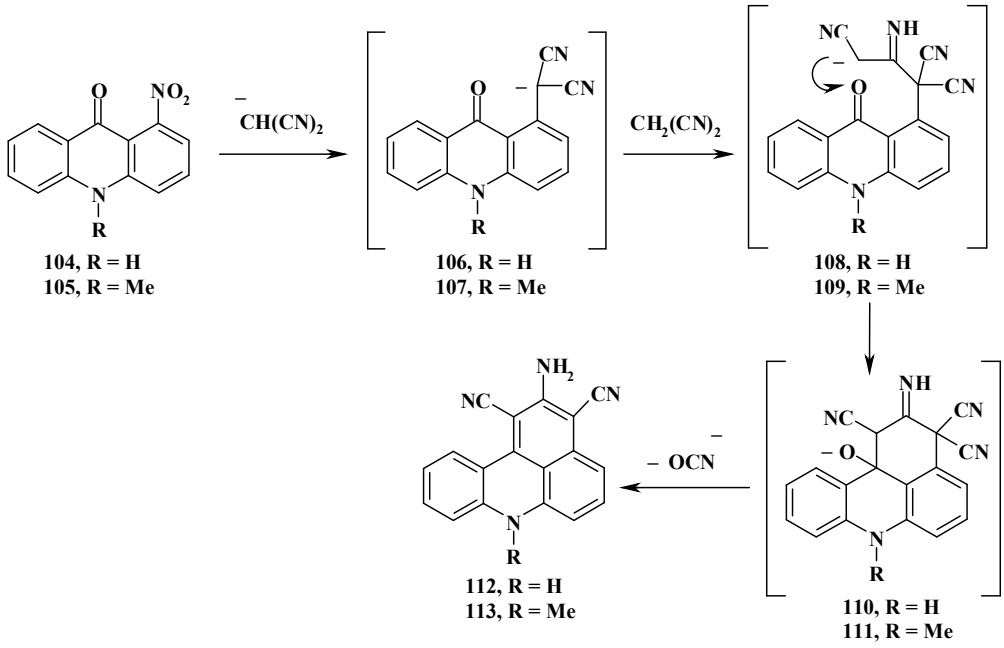
Malononitrile 1 on condensation with *cis*-2,6-diarylpiperidin-4-ones 94 and 95, *t*-(3)-methyl-*r*(2),*c*(6)-diarylpiperidin-4-ones 96 and 97 and *t*(3),*t*(5)-dimethyl-*r*(2),*c*(6)-diphenylpiperidin-4-one 98 yielded the expected 4-dicyanom- ethylene derivatives 99-103. [57]



94-98 99-103

	Ar	R1	R2		Ar	R1	R2
94	Ph	H	H	99	Ph	H	H
95	*o*-ClC_6H_4	H	H	100	*o*-ClC_6H_4	H	H
96	Ph	CH_3	H	101	Ph	CH_3	H
97	*p*-$CH_3OC_6H_4$	CH_3	H	102	*p*-$CH_3OC_6H_4$	CH_3	H
98	Ph	CH_3	CH_3	103	Ph	CH_3	CH_3

Reaction of malononitrile 1 with 1-nitro and 10-methyl-1-nitro-9- acridone 104 and 105 leads directly to the corresponding 2-amino-1,3-dicyanoben- zo[*kl*]acridines 112 and 113. A solution of 1-nitro-9-acridone 104 or 10-methyl-1-nitro-9-acridone 105 in DMF was added to a solution of malononitrile sodium salt, obtained by the reaction of malononitrile and sodium hydride in DMF. These were stirred for 2h at 100-105°C. The adducts 2-Amino-1,3-dicyanobenz[*kl*]acridine 112 or 2-amino-1,3-dicyano-7-methylbenz[*kl*]acridine 113 were obtained. [58]



104, R = H
105, R = Me

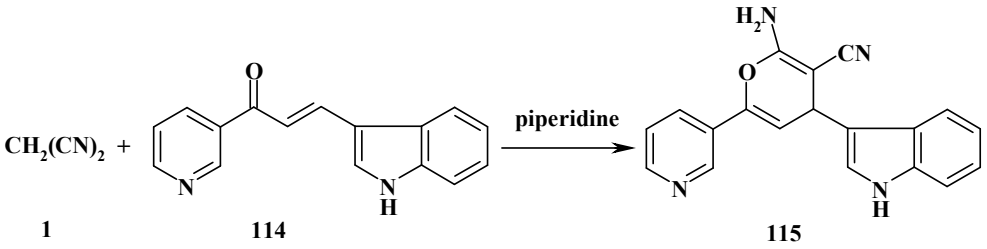
106, R = H
107, R = Me

108, R = H
109, R = Me

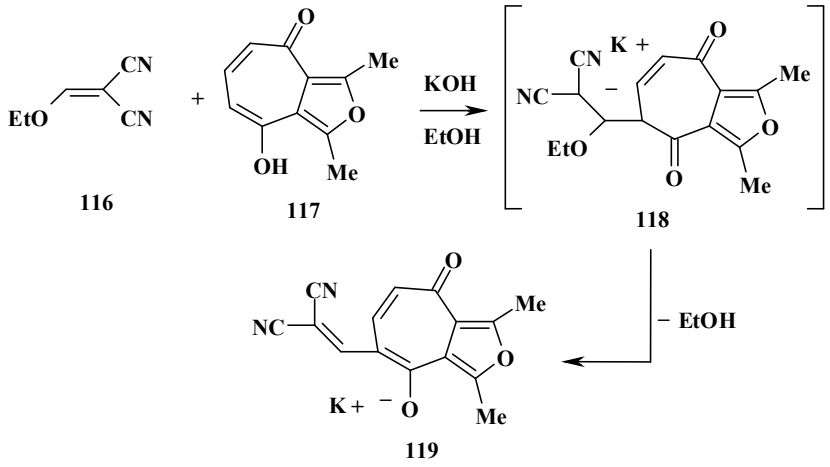
112, R = H
113, R = Me

110, R = H
111, R = Me

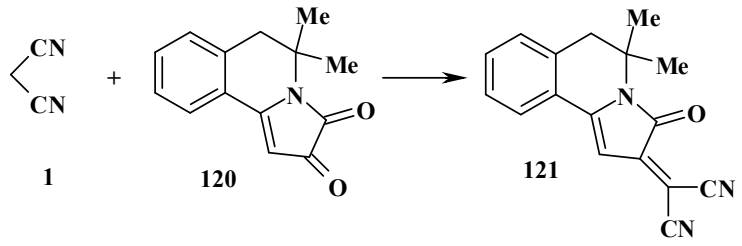
2-Amino-4-(3-indolyl)-6-(3-pyridyl)-pyran-3-carbonitrile 114 was prepared by condensation of malononitrile 1 and the α,β-unsaturated ketone 115 in the presence of piperidine as a catalyst in refluxing ethanol. [59]



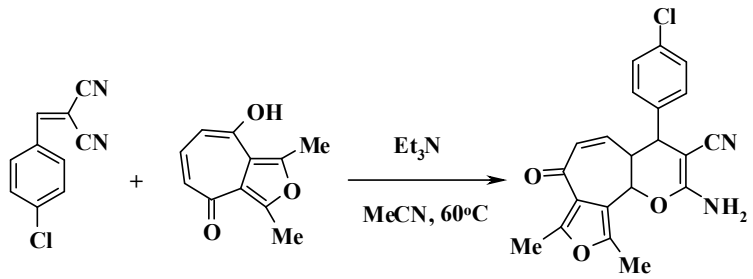
It was found that ethoxymethylenemalononitrile 116 reacts readily with 8-hydroxytropone 117 but not to give the expected 2*H*-pyran-2-one but the noncyclic vinyl derivative as its potassium salt 119 via the intermediate 118. [60]



Malononitrile 1 reacts with 5,5-dimethyl-2,3,5,6-tetrahydropyrrolo[2,1-*a*] isoquinoline-2,3-dione 120 in benzene in the presence of piperidine and acetic acid by heating under reflux for 5 min. to furnish 2-(5,5-dimethyl-3-oxo-2,3,5,6-tetrah-ydropyrrolo-[2,1*a*]isoquinolin-2-ylidene)malononitrile 121. [61]

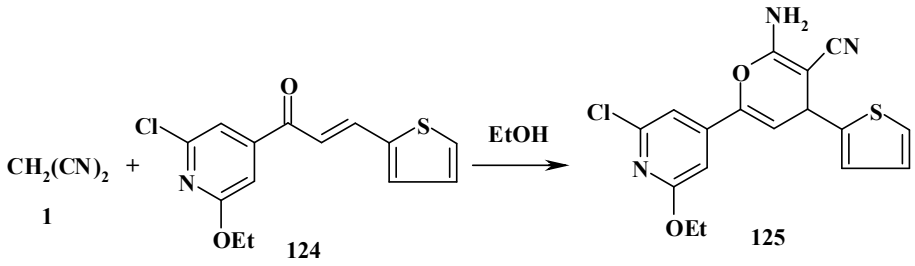


It is found that malononitrile derivative 122 reacts readily with hydroxytrop- one 117 with the formation of the expected 2-amino-4*H*-pyran 123. The reaction takes place under mild conditions in acetonitrile at 50-60^{o}C after the addition of catalytic amounts of piperidine or triethylamine. [62]

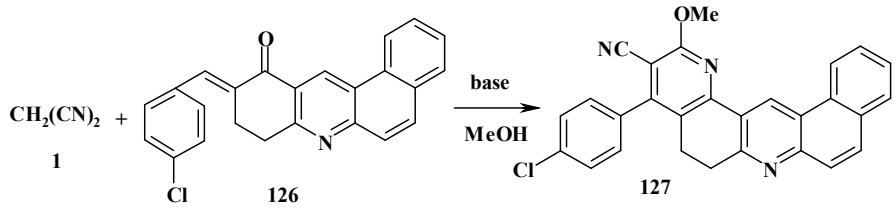


122 117 123

Treatment of α,β-unsaturated ketone 124 with malononitrile in refluxing ethanol with a small amount of piperidine gave the cyanoaminopyrane 125. [63]

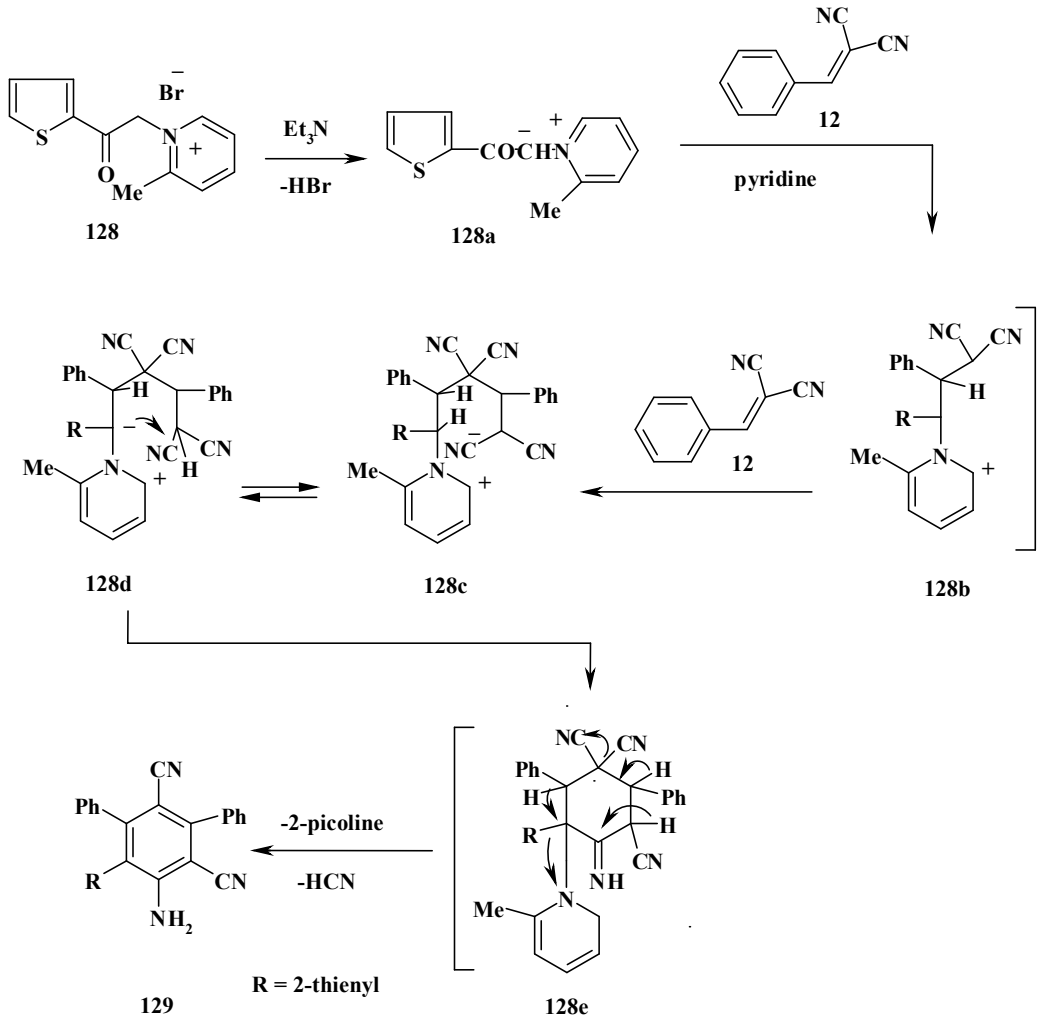


Malononitrile 1 reacts with α,β-unsaturated ketone 126 in boiling methanol or ethanol in the presence of 50% aqueous potassium hydroxide. The final product was partially hydrogenated 2-methoxy (or ethoxy)-4-(*p*-chlorophenyl)-5,6-dihydronaphtho[2,1-*j*] [1,7] phenanthroline-3-carbonitrile 127. The alkoxy group in the finally product corresponding to the alcohol in which the condensation occured. [64]

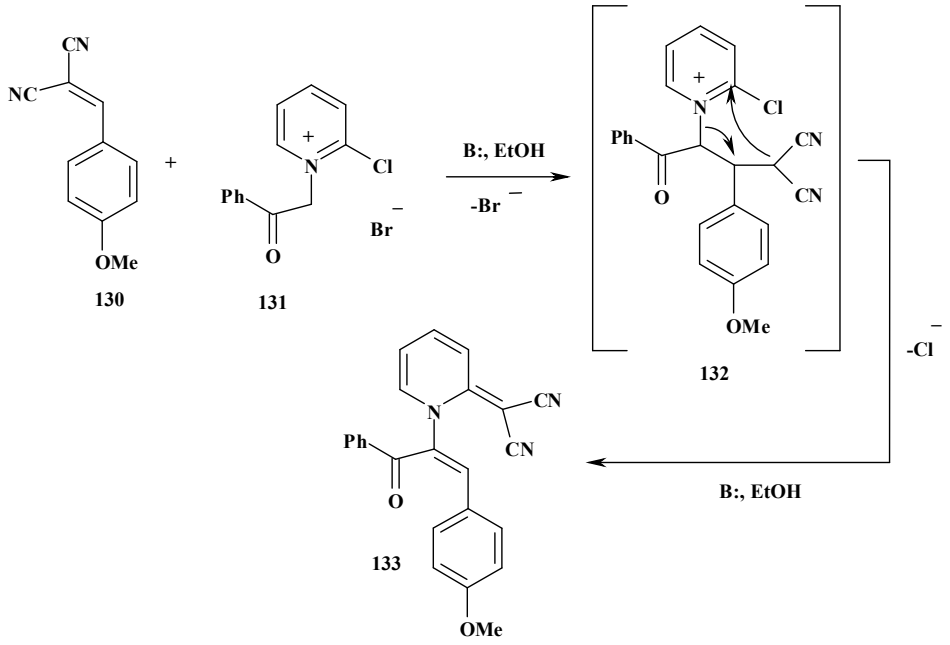


2.3 REACTION WITH HETEROCYCLIC COMPOUNDS

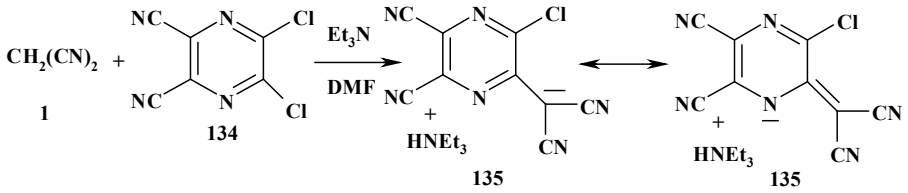
Reaction of benzylidenemalononitrile 12 with 1-(thiophene-2-yl)-1-oxo-ethane-2-picolinium bromide 128 in refluxing pyridine was investigated. This reaction afforded aniline derivative 129. [65]



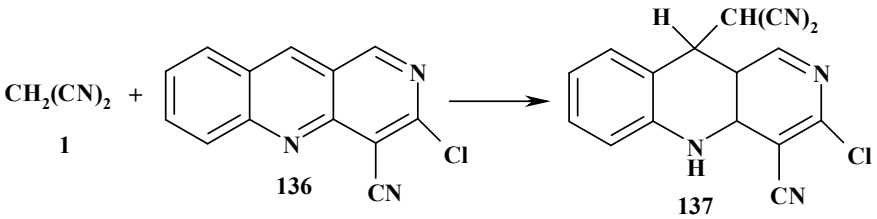
Reaction of *p*-methoxyphenylmethylenemalononitrile 130 with 1-(benzoylm-ethyl)-2-chloropyridinium bromide 131 in the presence of a twofold excess of a tertiary base to give 1-(1-benzoyl-2-*p*-methoxyphenylvinyl)-2-dicyanomethylene-1,2-dihydropyridine 133 the reaction occurs under mild conditions, probably *via* intermediate 132. [66]



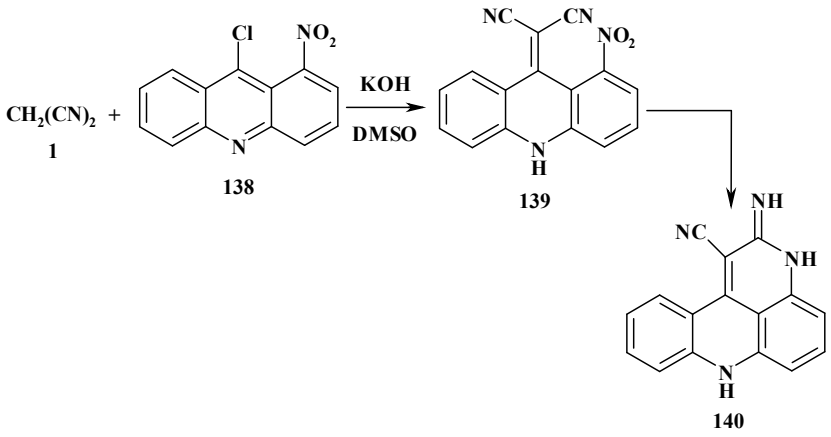
Malononitrile 1 reacts readily with 5,6-dichloro-2,3-pyrazine dicarbonitrile 134 at room temperature in DMF in the presence of triethyamine to form the salt 135. [67]



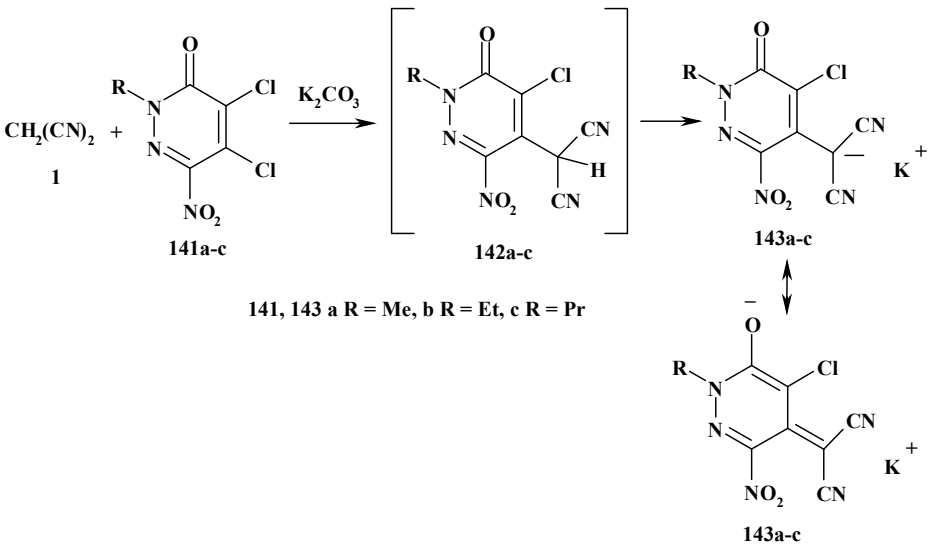
The reaction of malononitrile 1 with 3-chloro-4-cyanobenzo [*b*][1,6]naphtha- ayridine 136 in DMF with stirring for 5 days gives the adduct 3-chloro-4-cyano-10-dicyanomethyl-5,10-dihydrobenzo[*b*][1,6]naphthayridine 137. [68]



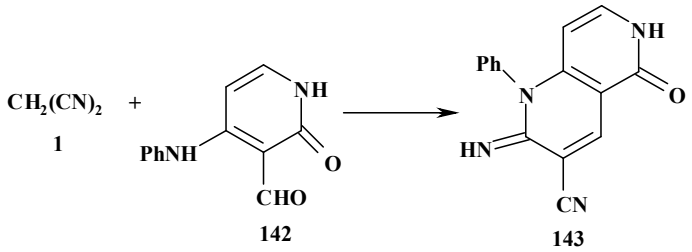
Malononitrile 1 reacts with 9-chloro-1-nitroacridine 138 in DMSO in the presence of KOH by stirring to give 9-dicyanomethylidene-1-nitro-9,10-dihydroacridine 139. On acidification of the adduct 139, it gives 1-cyano-2-imino-2,3-dihydro-7*H*-pyrido[2,3,4-*kl*]acridine 140. [69]



Treatment of 1-alkyl-4,5-dichloro-3-nitropyridazin-6-ones 141a-c with *C*-nucleophiles (such as the carbanion generated from malononitrile in the presence of potassium carbonate base) leads to a selective substitution of a chlorine atom by the quaternary carbon atom of the carbanion formed from malononitrile. Finally the potassium salts of 2-(1-alkyl-5-chloro-3-nitro-6-oxo-1,6-dihydro-4-pyrida- zinyl)malononitriles 143a-c were isolated. [70]

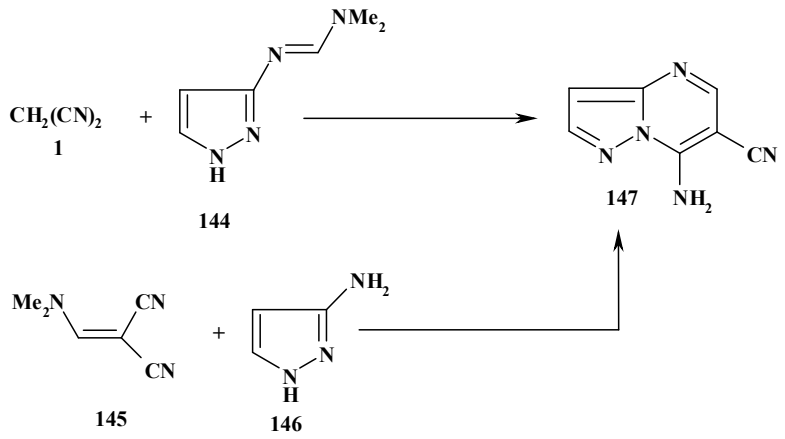


The reaction of malononitrile 1 with 3-formylpyridone 144 in the presence of Et_3N both in ethanol and pyridine produces 2-iminonaphthyridin-5-one 145. [71]

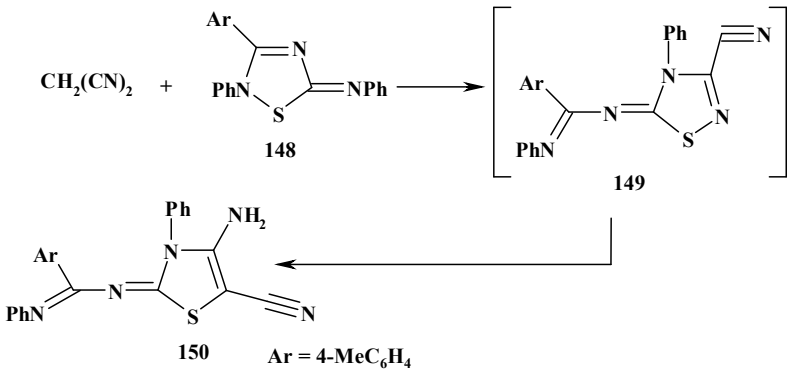


Treatment of malononitrile 1 with *N,N*-dimethyl-*N*-(1*H*-pyrazol-3-yl)forma-midine 144 yielded 7-aminopyrazolo[1,5-*a*]pyrimidine-6-carbonitrile 147. [72]

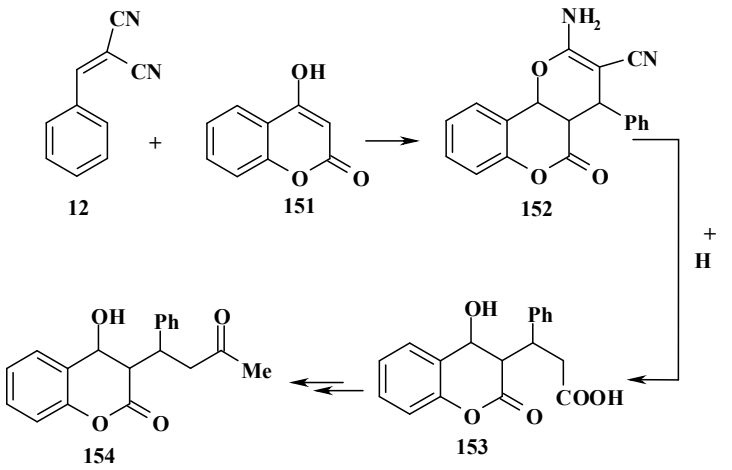
Also the adduct 147 can be obtained by reaction of malononitrile 1 derivative dimethylaminomethylidenemalononitrile 145 with 3-aminopyrazole 146 in refluxing ethanol in the presence of piperidine. [73]



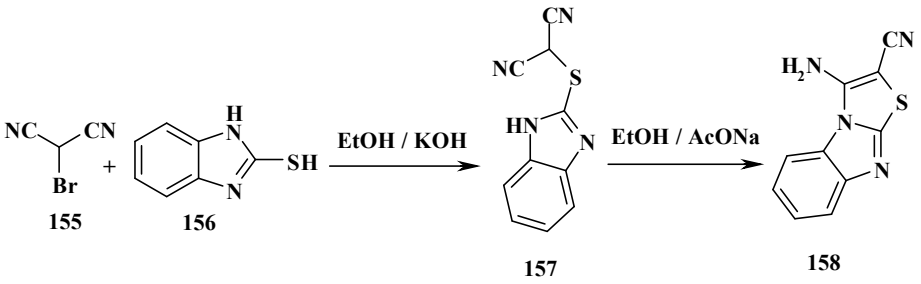
Reaction of malononitrile 1 with substituted 1, 2, 4-thiadiazol-5(2*H*)-imines 148 in refluxing dioxane gives *N'*-[4-amino-3-phenyl-5-cyanoth-iazol-2(3*H*)-ylidene]-4-methyl(methoxy)-N^2-phenylbenzamidines 150 *via* intermediate 149. [74]



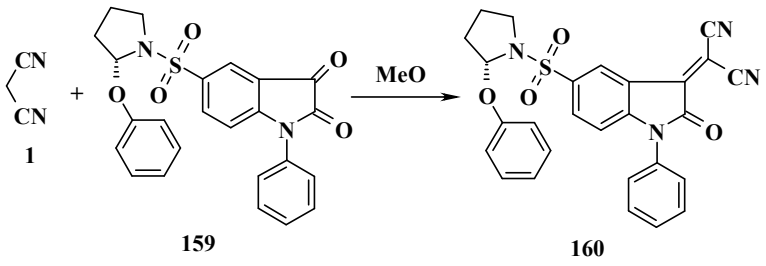
Heating of malononitrile 1 derivative benzylidenemalononitrile 12 with 4-hydroxycoumarin 151 in pyridine or water leads to the formation of 2-amino-3-cyano-5-oxo-4-phenyl-4,5-dihydropyrano[3,2-*c*] chromene 152. Acid hydrolysis of substituted pyrano[3,2-*c*]chromene 152 gives the adduct 153, which is used to synthesize warfarin 154. [75]



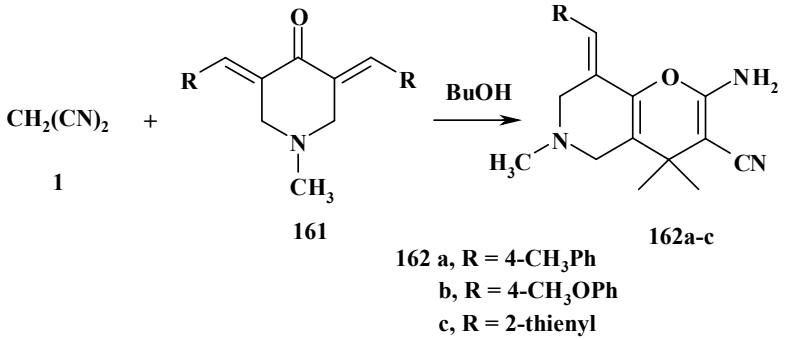
3-Aminothiazolo[3,2-a]benzimidazol-2-carbonitrile 158 was prepared by the reaction of 2-mercabtobenzimidaziole 156 with bromomalononitrile 155 in ethanol followed by cyclization reaction of product 157 in the presence of anhydrous sodium acetate. [76-79]



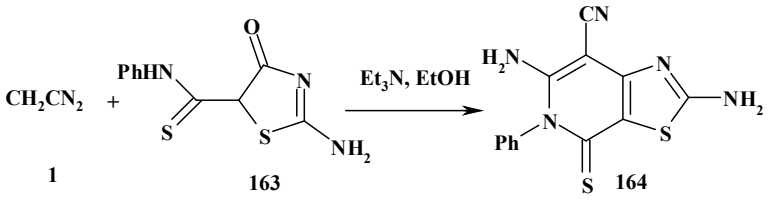
By condensing malononitrile 1 with isatinsulfonamide 159 in methanol, the adduct 160 was formed. [80, 81]



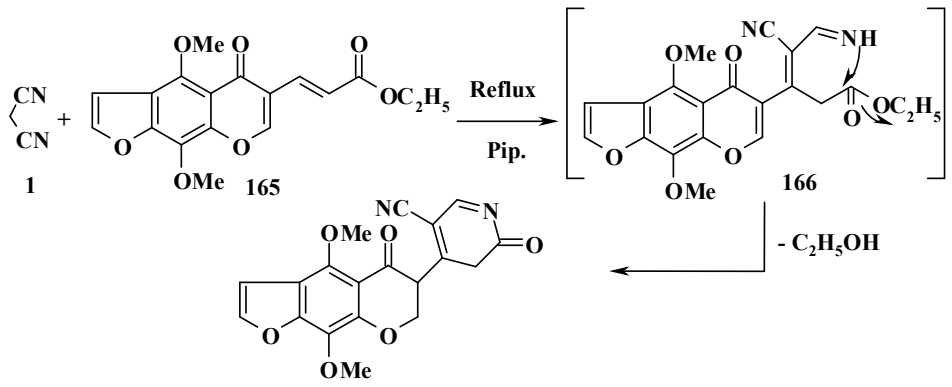
On reaction of malononitrile 1 with piperidone derivatives 161, the pyrano [3,2-c]pyridines 162 were obtained. [82]



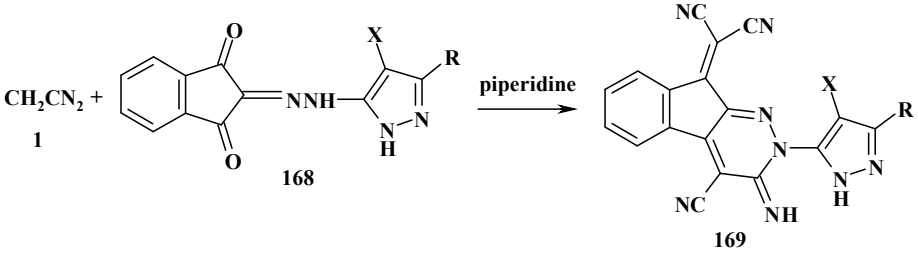
On treatment of malononitrile 1 with 2-imino-5-phenylaminothiocarboxamido-4-thiazolidone 163, a thiazolopyridine 164 was obtained. [83]



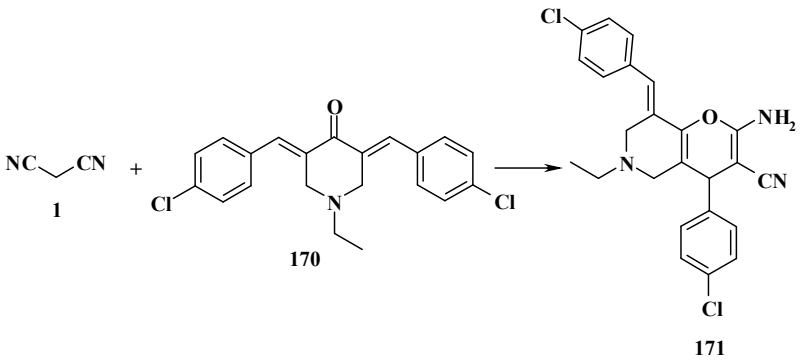
Refluxing of malonitrile 1 with furochromenethylacrylate 165 in ethanol in presence of catalytic amount of pipredine formed 4-(4,9-dimethoxy-5-oxo-5*H*-furo [3,2-*g*]chromen-6-yl)-6-oxo-5,6-dihydropyridi-ne-3-carbonitrile 167 *via* 166. [84]



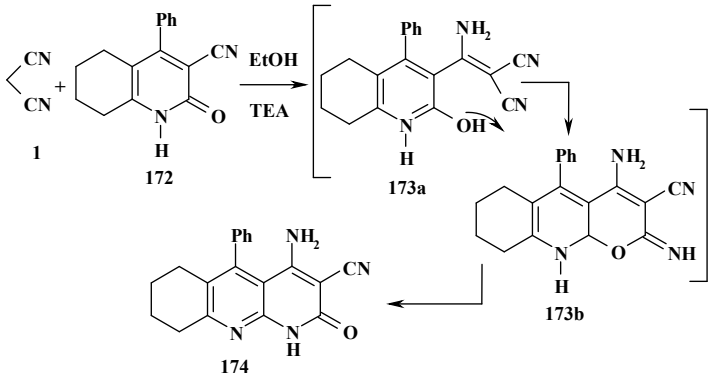
Reaction of malononitrile 1 with 2-(3-methylpyrazol-5-yl)hydrazono-1,3-indanedione 168 in boiling ethanol in the presence of piperidine gave indeno[2,1-*c*]pyridazine-4-carbonitrile derivatives 169a,b. [85]



Malononitrile 1 reacts with 3,5-bis(benzylidene)-1-ethylpiperidin-4-ones 170 to give pyranopyridine derivative 171. [86]

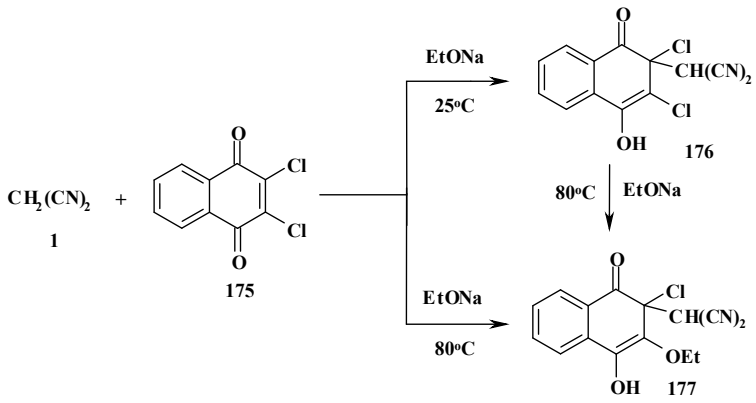


Malononitrile 1 was refluxed with hexahydroquinoline 172 to afford 4-amin-obenzo[*b*]-[1,8]napthyridine-3-carbonitrile 174 via the intermediates 173a and 173b. [87]

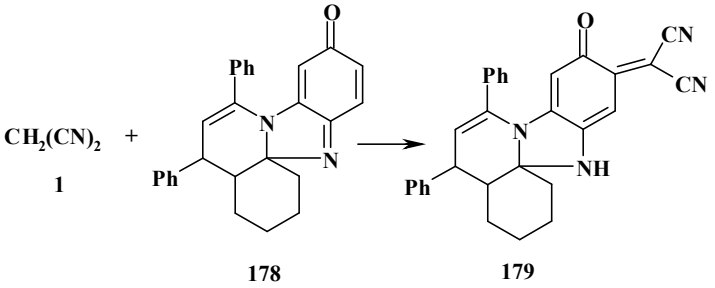


2.4 REACTION WITH QUINONES

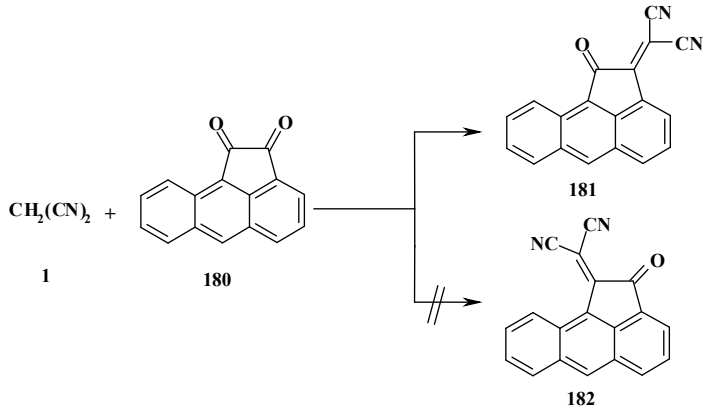
Malononitrile 1 reacts with 2,3-dichloro-1,4-naphthoquinone 175 in equimolar ratios in the presence of an equivalent amount of sodium ethoxide at room temperature and ethanol as reaction medium to give (2,3-dichloro-4-hydroxy-1-oxo-1,2-dihydro-2-naphthalenyl)-propanedinitrile 176. On carrying out this reaction in refluxing ethanol, two different products were formed, (2-chloro-3-ethoxy-4-hydroxy-1-oxo-1,2-dihydro-2-naphthalenyl) propanedinitrile 177 and the other product was identified as dinitrile 176. Compound 177 is expected to be formed *via* 176. [88]



A two fold molar excess of malononitrile 1 was added with stirring to a suspension of quinoneimine 178 in refluxing ethanol, this led to formation of 8-dicyanomethylene-7-oxo-2,4-diphenyl-1,2,7,8-tetrahydro-1,10*a*-cyclohexanopyrid- o[1,2-*a*] benzimidazole 179. [89]

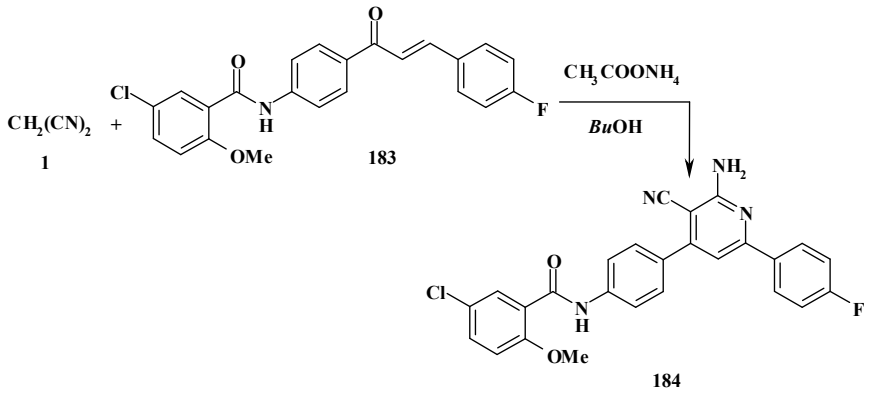


Treatment of malononitrile 1 with aceanthrenequinone 180 in dimethylform- amide at reflux afforded 2-(dicyanomethylene)aceanthren-1-one 181 and not 182. [90]

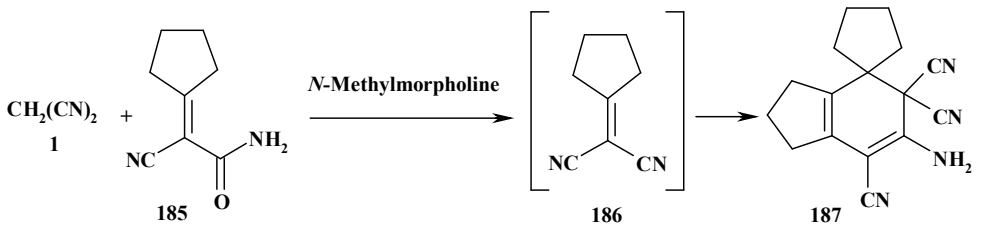


2.5 REACTION WITH AMIDES

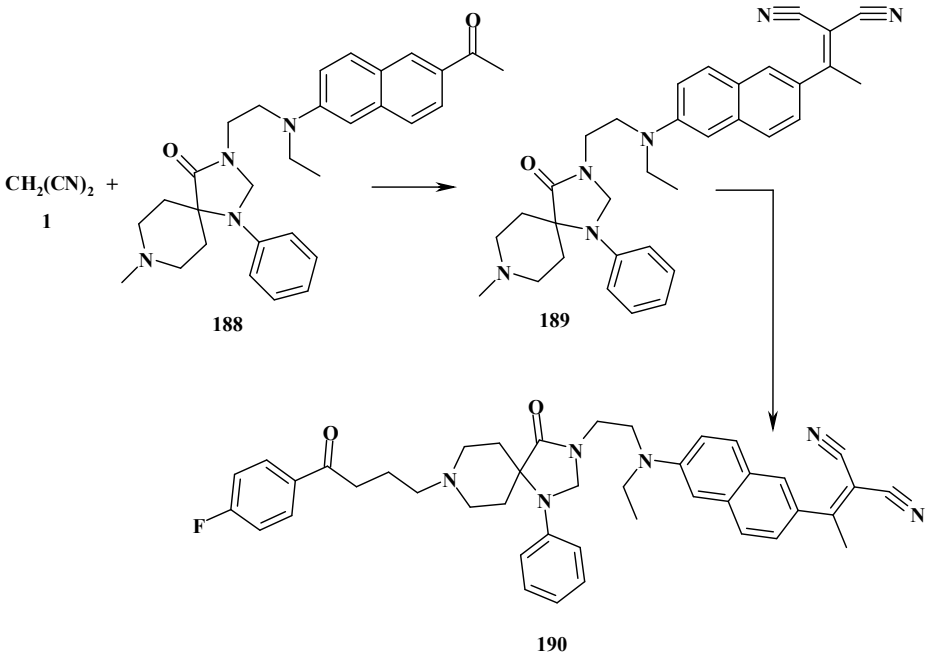
Condensation of malononitrile 1 with *N*1-[4-(4-fluorocinnamoyl)phenyl]-5-chloro-2-methoxybenzamide 183 in refluxing *n*-butanol in the presence of ammonium acetate gave cyanoaminopyridine 184. [91]



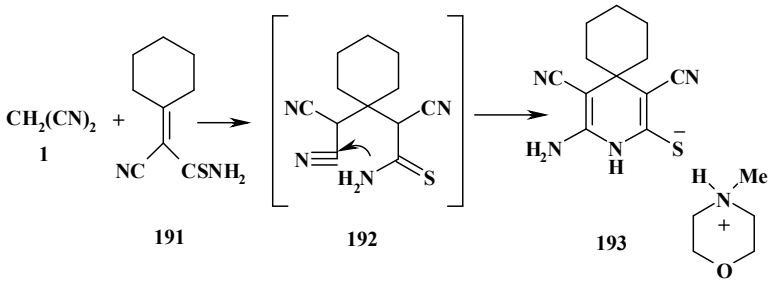
It is found that malononitrile 1 reacts with cyclopentylidene(cyano) acetamides 185 at 20°C in ethanol in the presence of *N*-methylmorpholine to give spirocyclohexadiene 187. The reaction is likely to involve intermediate formation of cyclopentylidenemalononitrile 186 as a result of exchange of the methylene components: the cyanoacetamide moiety is replaced by malononitrile fragment. Compounds 186 undergo cyclodimerization in the presence of a base. [92]



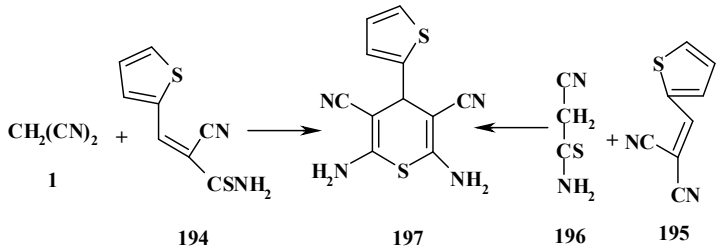
Reaction of malononitrile 1 with amide 188 in refluxing pyridine gave the adduct 189 which upon acid catalyzed deprotection of spiperone moiety gave the new *Vis* wavelength fluorescent probe 190. [93]



Reaction of malononitrile 1 with cyano(cyclohexaylidene)thioacetamide 191 in the presence of *N*-methylmorpholine and as a result of subsequent intra- molecular cyclocondensation, under the action of a base (*N*-methylmorpholine), the adduct 192 transforms into 193. [94]



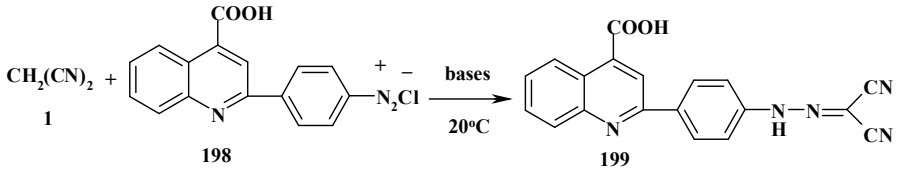
It is found that reaction of malononitrile 1 with 2-thienylidene derivative of cyanothioacetamide 194 in alcohol under the action of organic bases at 20°C resulted in the formation of 4*H*-thiopyran 197. Also the adduct 197 can be prepared by reaction of malononitrile 1 derivative (2-thienylidenemalononitrile) 195 with cyanothioacetamide 196. [95]



194 197 196 195

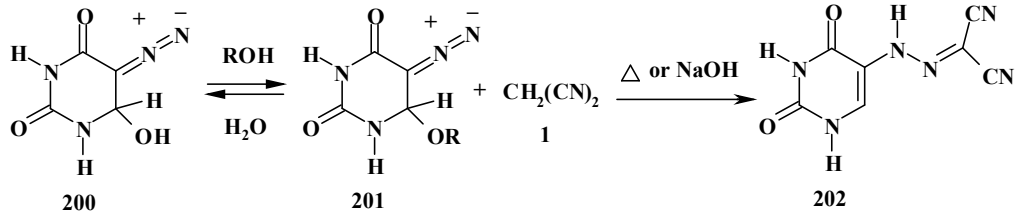
2.6 REACTION WITH DIAZACOMPOUNDS

Condensation of malononitrile 1 with aryldiazonium salt 198 readily occurs at 20°C to give hydrazone 199. [96]



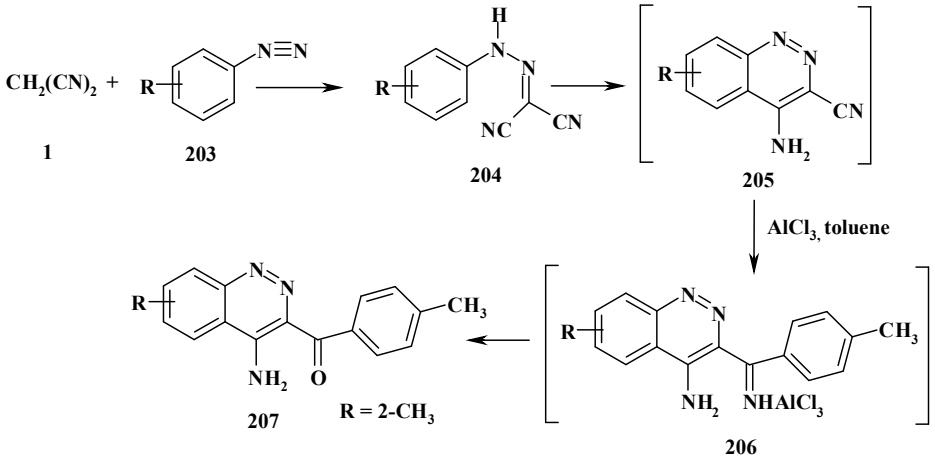
198 199

Coupling of malononitrile 1 with 6-hydroxy-5-diazouracil 201 in ethanol or methanol in the presence of NaOH and boiling gives the adduct 202. [97]



200 201 202

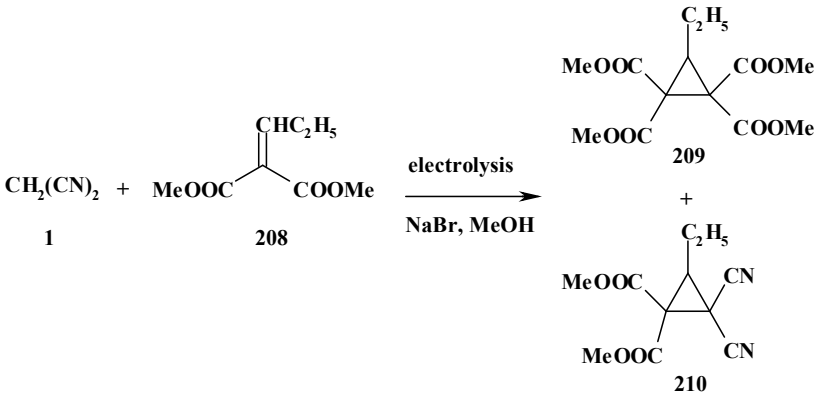
Treatment of malononitrile 1 with diazonium salt 203 gives hydrazonomalononitrile 204. On refluxing 204 with $AlCl_3$ in toluene it gives (4-aminocinnolin-3-yl)-*p*-tolylmethanone 207 *via* intermediates 205 and 206. [98]



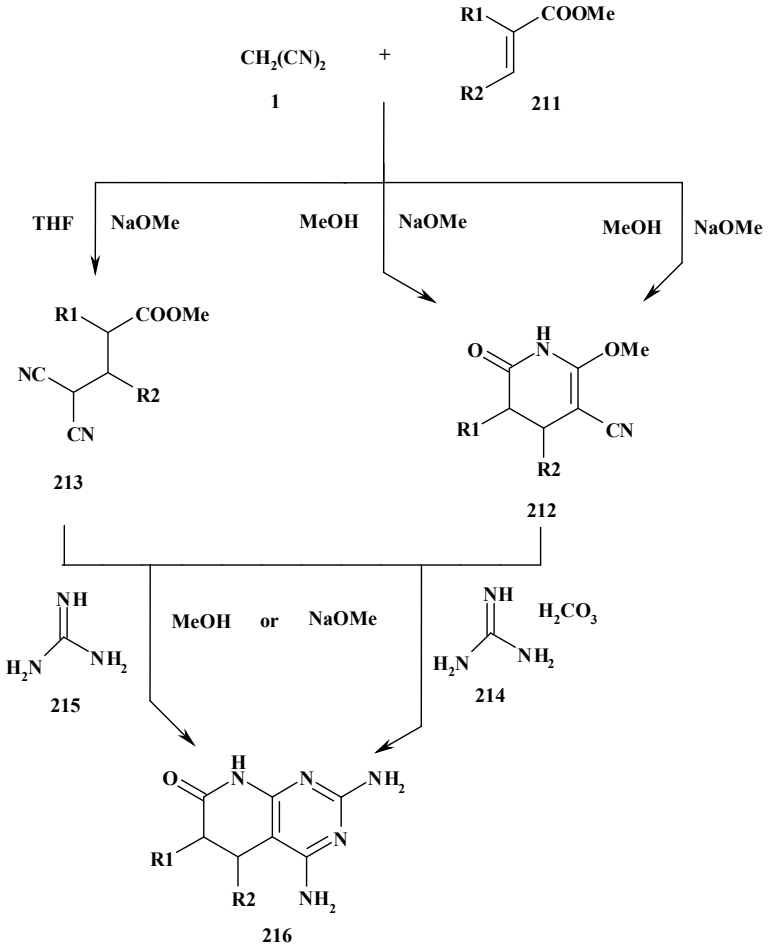
1 203 204 205 206 207 R = 2-CH_3

2.7 REACTION WITH ESTERS

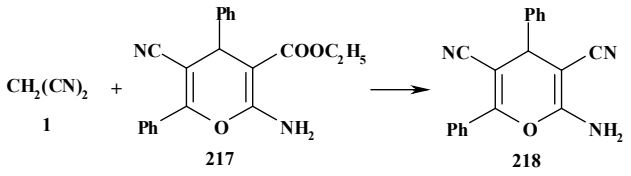
The combined electrolysis of malononitrile 1 and ethylidenemalonate 208 at temperature 20, 10, 0°C afforded tetra ester 209 along with dicyano derivative 210. [99]



Condensation of malononitrile 1 with α, β-unsaturated ester211 [100], [101] in NaOMe/MeOH followed by intra molecular cyclization yields pyridones 212 and subsequent treatment with guanidine carbonate 214 in NaOMe/MeOH or guanidine 215 in methanol gives the adduct 216. But on treatment of malononitrile with α, β-unsaturated ester 211 in NaOMe/THF gives the adduct 213 which on addition of guanidine carbonate 214 in NaOMe/MeOH or guanidine 215 in methanol leads to formation of the adduct 216. [102], [103]



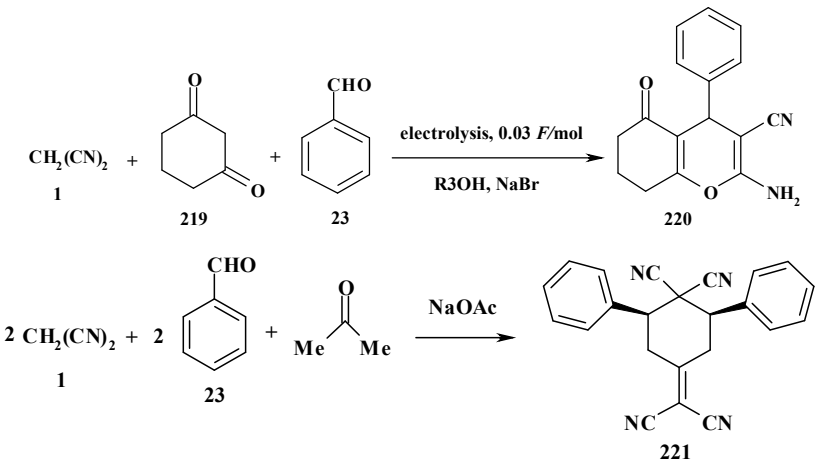
Treatment of malononitrile 1 with β-enaminoester 217 in refluxing ethanol yields 2-amino-3, 5-dicyano-4, 6-diphenyl-4*H*-pyran 218. [104]



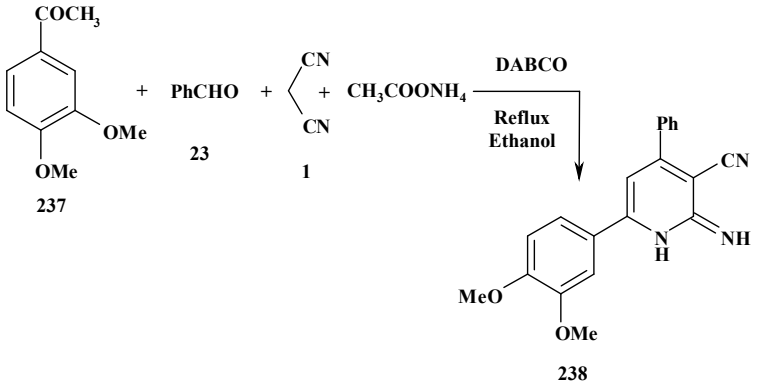
2.8 A One-Pot Multi-Component Reaction

Different pyran derivatives were synthesized by a one-pot reaction mixture composed of multi-component under different conditions.[56], [105-131]

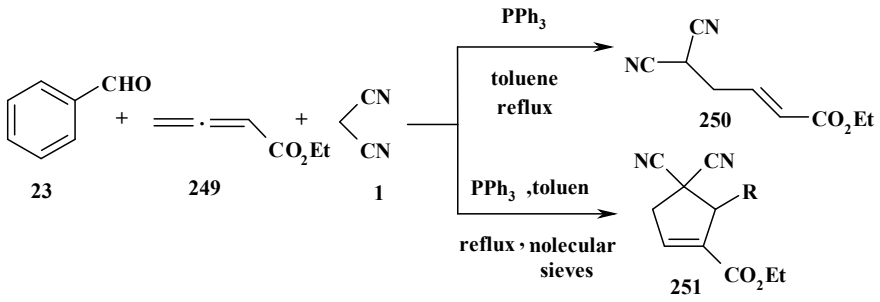
A base-catalyzed transformation of malononitrile 1, benzaldehyde 23 and acetone into diphenylcyclohexane 221 was achieved in highest yield in the presence of KF. The formation of compound 221 was also detected in the reactions catalyzed by KOAc, Na_2CO_3, and K_2CO_3. [105]



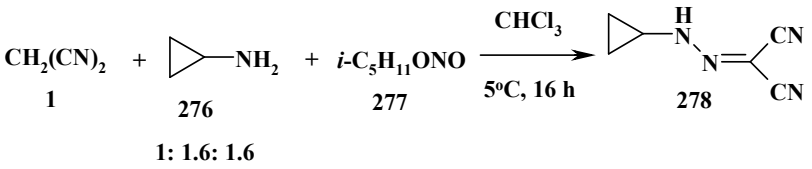
Reaction of malononitrile 1, 3,4-dimethoxyacetophenone 237, ammonium acetate and benzaldehyde 23 in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO) in ethanol gave pyridine derivative 238. [131-141]



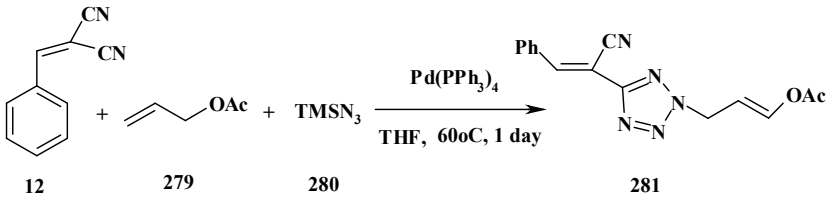
It was found that when malononitrile 1 was treated with benzaldehyde 23 and 2,3-butadienoate 249 in toluene in the presence of triphenylphosphine, malononitrile reacted with 2,3-butadienoate only to give 250 but when molecular sieves were used the reaction was performed as a one-pot synthesis consists of three component and a cyclic adduct 251 is obtained. [142]



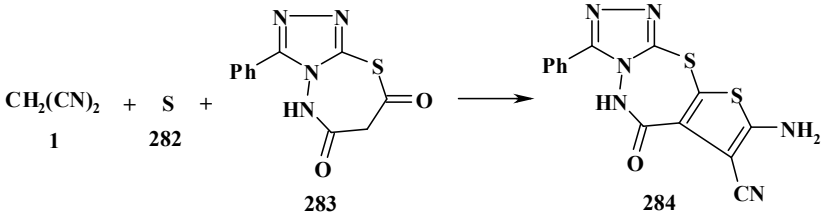
Malononitrile can react with cyclopropyldiazonium to give azo compounds. The reaction of isoamyl nitrite 277 with a mixture of cyclopropylamine 276 and malononitrile 1 in $CHCl_3$ affords the expected cyclopropylhydrazone 278. [143]



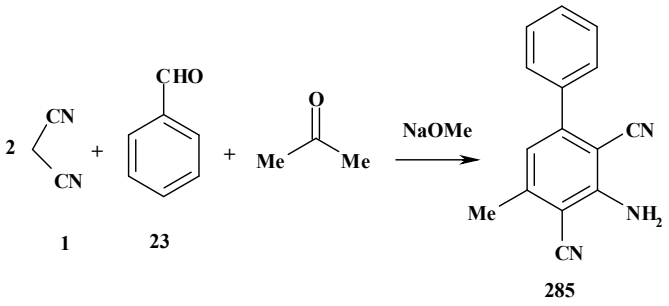
The synthesis of tetrazoles was achieved *via* palladium-catalyzed three component coupling (TCC) reaction. The (TCC) reaction of malononitrile derivative 12, allyl acetate 279 and trimethylsilyl azide 280 proceeds very smoothly under a catalytic amount of $Pd(PPh_3)$ to give 2-allyltetrazole 281. [144], [145]



One-pot reaction of malononitrile 1 with sulfur 282 and 3-phenyl-5,6,7,8-tetrahydro[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazepine-6,8-dione 283 in DMF and in the presence of Et_3N as catalyst at room temperature yielding thiophenotriazolo- thiadiazepine derivative 284. [146]



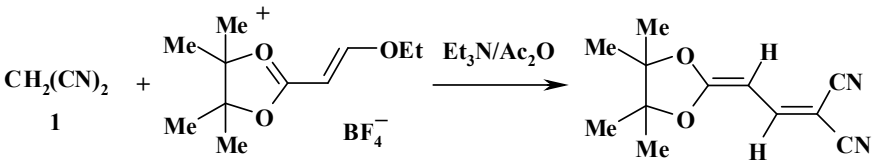
Amino-2,4-dicarbonitrile-5-methylbiphenyls are synthesized by a three-component, thus the reaction of aromatic aldehydes, malononitrile, and acetone in the presence of catalytic NaOMe under grindstone method. The yields are excellent; the procedure is simple, efficient, and environmentally benign; and all the reactions go to completion within 2–3min. [147]



1 23 285

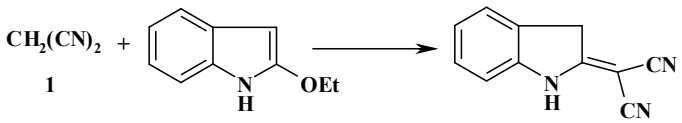
2.9 REACTION WITH ETHERS

Reaction of malononitrile 1 with ether 286 in refluxing acetic anhydride in the presence of triethylamine. As a result, the corresponding cyanomethylene derivative 287 was obtained. [148]



1 286 287

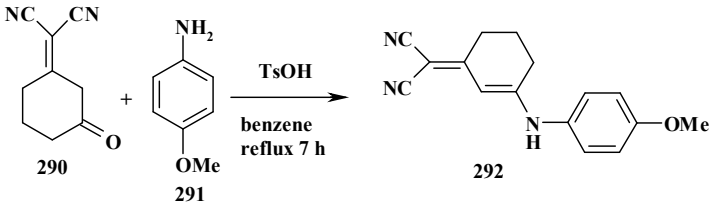
A mixture of malononitrile 1 and ether 288 was heated at 100- 110°C with distillation of the forming alcohol until the reaction was over (the distillation ceased). Finally the adduct 2-dicyanomethylidene 289 was obtained. [149]



1 288 289

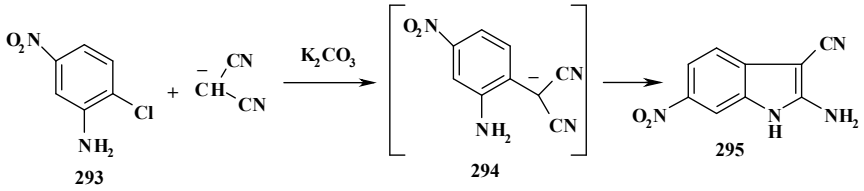
2.10 REACTION WITH AMINES

Malononitrile 1 derivative (3-oxocyclohexyl-1-idene)malononitrile 290 reacts with *p*-anisidene 291 in boiling benzene in the presence of TsOH to give [3-(4-methoxyphenylamino)-2-cyclohexenylidene]malononitrile 292. [150]

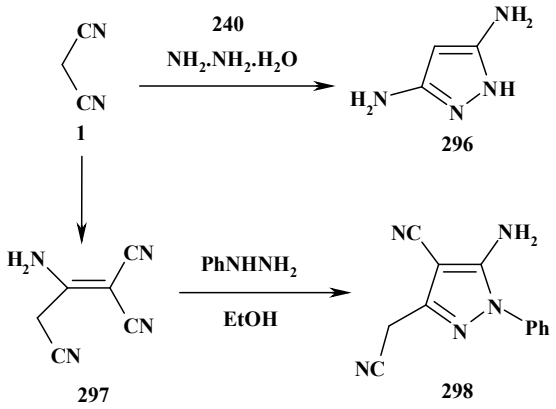


290 291 292

2-Amino-6-nitroindole 295 was obtained by reaction of carbanion generated from malononitrile by action of base with 2-chloro-5-nitroaniline 293 *via* intermediate 294. [151]

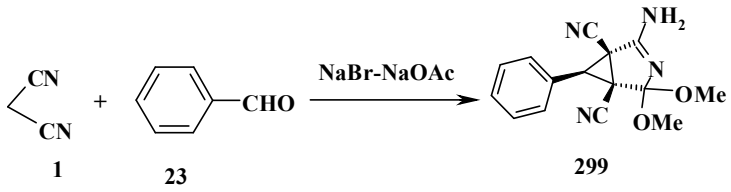


It has been reported in old German literature [152] that malononitrile 1 reacted with hydrazine hydrate 240 to yield 3,5-diaminopyrazole 296. Subsequently Sato, [153] Taylor, Hartke [154] and Elnagdi and co-workers [155] have established that the product was really 298; formed *via* initial dimerization of malononitrile 297. [156]

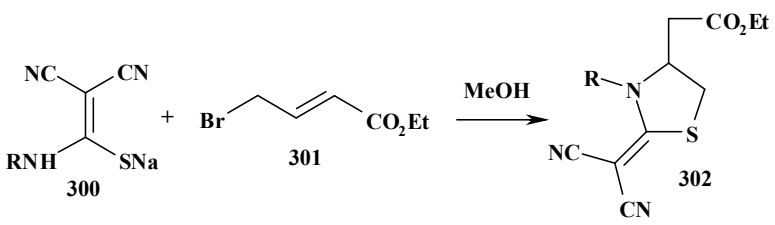


2.11 Reaction With Unsaturated Compounds

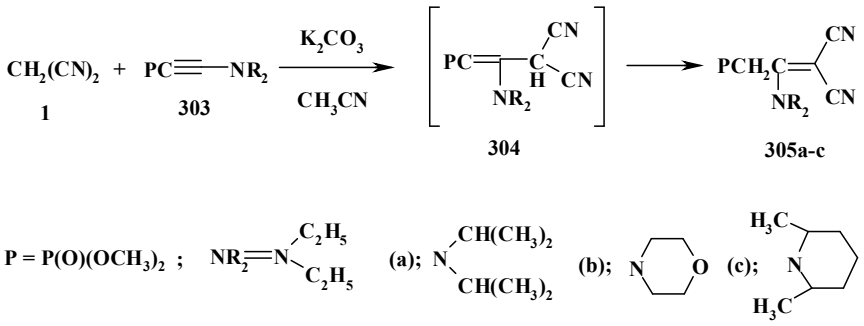
In one-pot stereoselective electrocatalytic domino transformation of malononitrile 1 and benzaldehyde 23 into 2-amino-1,5-dicyano-4,4-dimethoxy-6-phenyl-3-aza-bicyclo[3.1.0]hexa-2-ene 299 takes place. The process was carried out in an undivided cell in methanol or ethanol; NaBr or the new system NaBr-NaOAc is used as mediators. [25]



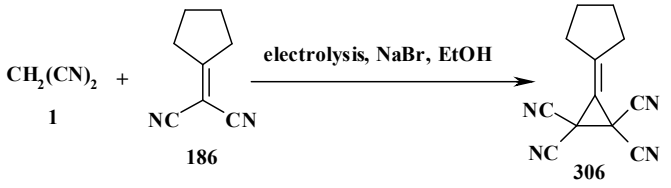
Reaction of malononitrile derivative 300 with 4-bromocrotonate 301 leads to the formation of thiazoles 302. [157]



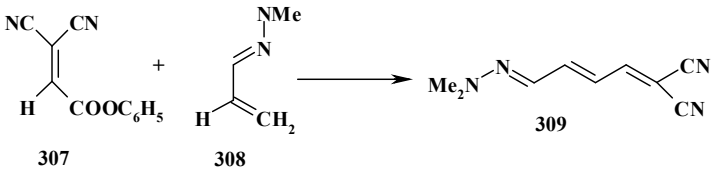
Malononitrile 1 reacts readily with aminoethynylphosphonate 303 in acetonitrile in the presence of potassium carbonate to give (2-amino-3,3-dicyan-oprop-2-enyl)phosphonate 305a-d *via* intermediate 304. [158]



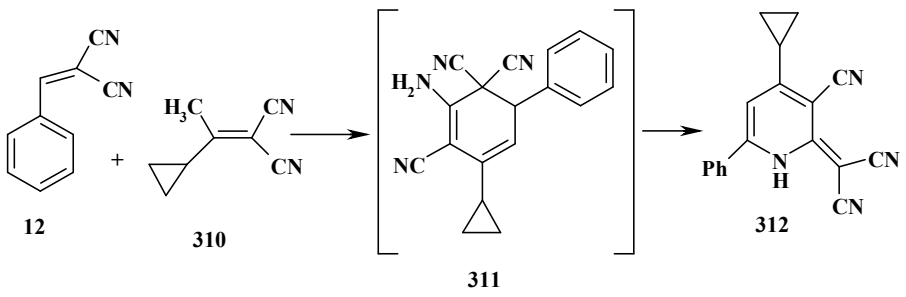
Electrolysis of malononitrile 1 and cyclopentylidenemalononitrile 186 in methanol in an undivided cell in the presence of the NaBr-NaOMe mediator system gives spirocyclic compound 306. [159]



The reaction between acyloxymethylidenemalononitrile 307 and α,β-unsatura- ted hydrazone 308 in benzene, by stirring affords 2-cyano-6-(*N'*,*N*'-dimethylhyd-razono)hexa-2,4-dienenitrile 309. [160]

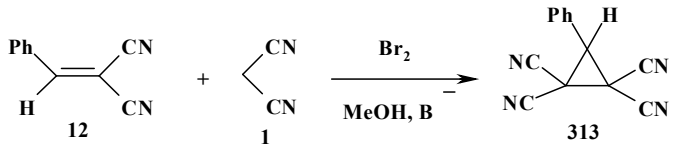


Benzylidenemalononitrile 12 was treated with (1-cyclopropylethylidene) malononitrile 310 in methanol in the presence of few drops of morpholine and by stirring for 0.5 h at 25°C to give 1-amino-5-phenyl-2,6,6-tricyano-3-cyclopropyl-1,3-cyclohexadiene 312 *via* thermal transformation of cyclohexadiene 311. [161]

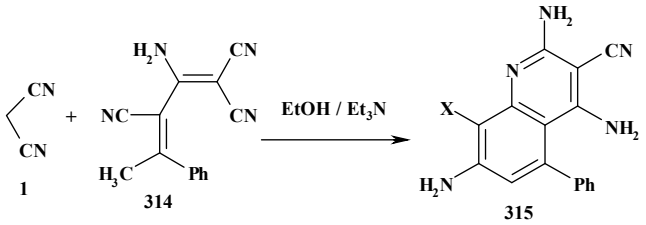


3-Phenyl-1,1,2,2-tetracyanocyclopropane 313 [162] was obtained in 95% yield through the reaction of 3-fold excess of benzylidenemalononitrile 12 with dibro-momalononitrile in the presence of equimolar quantity of rare indium powder and

0.2 equiv of lithium iodide as catalyst in dimethylformamide [163]. The next essential step in the cyclopropane ring construction was connected with the electrochemical technique and using halogen containing mediatory systems in an undivided cell. Thus, the new electrochemical approach to functionally substituted cyclopropanes was performed by the electrolysis of alkylidenemalonates and malonate in an undivided cell in methanol in the presence of halides as mediators. [164]



Malononirile 1 reacts with 2-amino-4-phenylpenta-1,3-diene-1,1,3-tricarboni- trile 314 to give 2,4,7-triamino-5-phenylquinoline-3,8-dicarbonitrile 315. [165]



3 CONCLUSION

Malononitrile plays an important role as a start material or reagent for synthesizing of many useful substances that are used in different fields of life. So the authors tried to make a survey and collect the data belong to this useful material.

ACKNOWLEDGEMENT

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